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NEWS 2 AUG 10 Time limit for inactive STN sessions doubles to 40
minutes
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(CS) field
NEWS 4 AUG 24 ENCOMPLIT/ENCOMPLIT2 reloaded and enhanced
NEWS 5 AUG 24 CA/CAplus enhanced with legal status information for
U.S. patents
NEWS 6 SEP 09 50 Millionth Unique Chemical Substance Recorded in
CAS REGISTRY
NEWS 7 SEP 11 WPIDS, WPINDEX, and WPIX now include Japanese FTERM
thesaurus

NEWS EXPRESS MAY 26 09 CURRENT WINDOWS VERSION IS V8.4,
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FILE 'HOME' ENTERED AT 23:09:45 ON 11 OCT 2009

=> file reg
COST IN U.S. DOLLARS SINCE FILE TOTAL
FULL ESTIMATED COST ENTRY SESSION
0.44 0.44

FILE 'REGISTRY' ENTERED AT 23:10:52 ON 11 OCT 2009
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STRUCTURE FILE UPDATES: 9 OCT 2009 HIGHEST RN 1187817-34-0
DICTIONARY FILE UPDATES: 9 OCT 2009 HIGHEST RN 1187817-34-0

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TSCA INFORMATION NOW CURRENT THROUGH June 26, 2009.

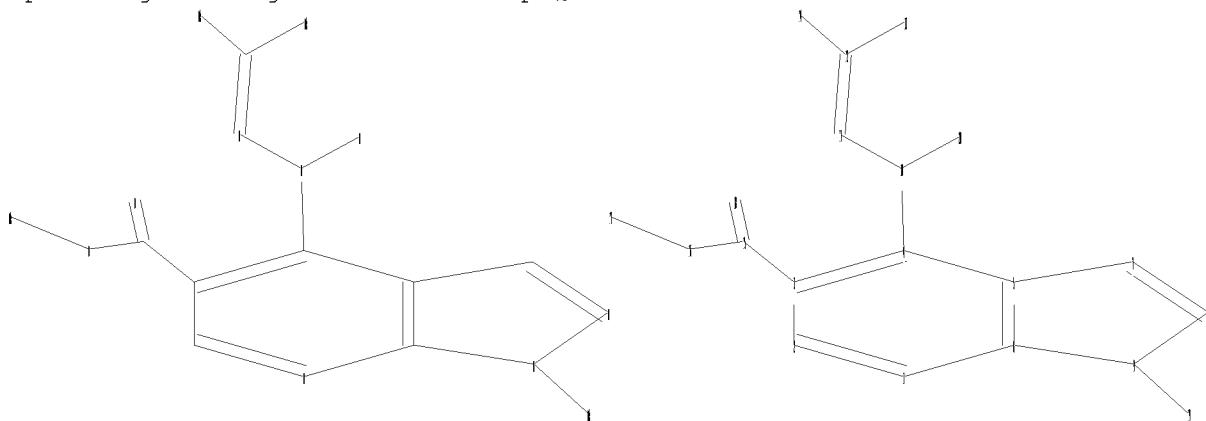
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<http://www.cas.org/support/stngen/stndoc/properties.html>

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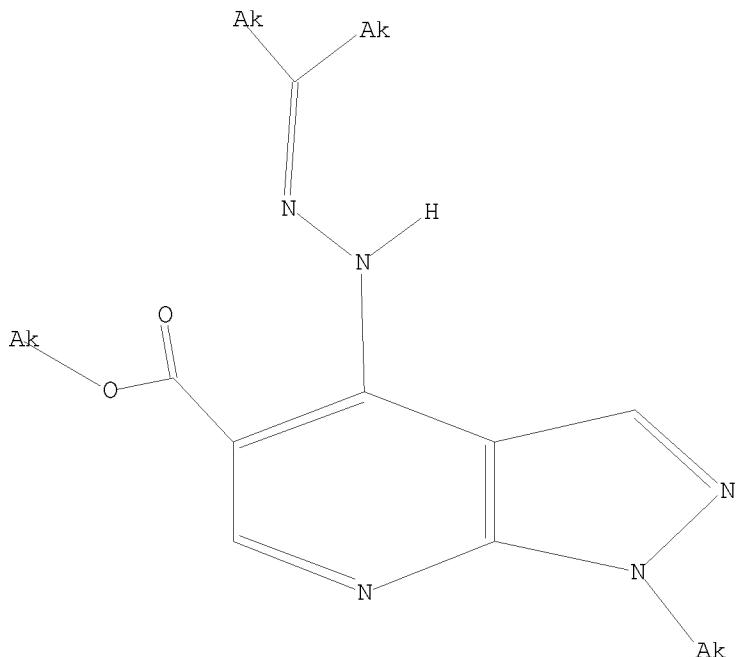


chain nodes :
10 11 12 13 14 15 16 17 18 19 20
ring nodes :
1 2 3 4 5 6 7 8 9
chain bonds :
3-15 4-10 9-19 10-11 10-20 11-12 12-13 12-14 15-16 15-18 16-17
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9
exact/norm bonds :
4-10 5-7 6-9 7-8 8-9 9-19 10-11 11-12 12-13 12-14 15-16 15-18 16-17
exact bonds :
3-15 10-20
normalized bonds :
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Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS

L1 STRUCTURE UPLOADED

=> d 11
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s 11 full
FULL SEARCH INITIATED 23:11:17 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 119 TO ITERATE

100.0% PROCESSED 119 ITERATIONS 28 ANSWERS
SEARCH TIME: 00.00.01

L2 28 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE TOTAL
FULL ESTIMATED COST ENTRY SESSION
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FILE 'CAPLUS' ENTERED AT 23:11:38 ON 11 OCT 2009
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FILE COVERS 1907 - 11 Oct 2009 VOL 151 ISS 16
FILE LAST UPDATED: 9 Oct 2009 (20091009/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2009

CAplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2009.

CAS Information Use Policies apply and are available at:

<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> s l2
L3      167 L2

=> s l3 and cognition
      19561 COGNITION
L4      6 L3 AND COGNITION

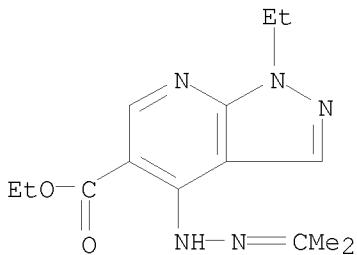
=> d 14 1-6 ibib abs hitstr

L4      ANSWER 1 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:      2008:827349 CAPLUS
DOCUMENT NUMBER:      149:167804
TITLE:                Etazolate, a neuroprotective drug linking GABAA
                      receptor pharmacology to amyloid precursor protein
                      processing
AUTHOR(S):            Marcade, Maryline; Bourdin, Jerome; Loiseau, Nadia;
                      Peillon, Helene; Rayer, Aurelie; Drouin, Dominique;
                      Schweighoffer, Fabien; Desire, Laurent
CORPORATE SOURCE:    Department of Neurology, ExonHit Therapeutics, Paris,
                      Fr.
SOURCE:              Journal of Neurochemistry (2008), 106(1), 392-404
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER:          Blackwell Publishing Ltd.
DOCUMENT TYPE:       Journal
LANGUAGE:            English

AB      Pharmacol. modulation of the GABAA receptor has gained increasing
attention as a potential treatment for central processes affected in
Alzheimer disease (AD), including neuronal survival and cognition
. The proteolytic cleavage of the amyloid precursor protein (APP) through
the  $\alpha$ -secretase pathway decreases in AD, concurrent with cognitive
impairment. This APP cleavage occurs within the  $\beta$ -amyloid peptide
(A $\beta$ ) sequence, precluding formation of amyloidogenic peptides and
leading to the release of the soluble N-terminal APP fragment (sAPP $\alpha$ )
which is neurotrophic and procognitive. In this study, we show that at
nanomolar-low micromolar concns., etazolate, a selective GABAA receptor
modulator, stimulates sAPP $\alpha$  production in rat cortical neurons and in
guinea pig brains. Etazolate (20 nM-2  $\mu$ M) dose-dependently protected
rat cortical neurons against A $\beta$ -induced toxicity. The
neuroprotective effects of etazolate were fully blocked by GABAA receptor
antagonists indicating that this neuroprotection was due to GABAA receptor
signaling. Baclofen, a GABAB receptor agonist failed to inhibit the
A $\beta$ -induced neuronal death. Furthermore, both pharmacol.
 $\alpha$ -secretase pathway inhibition and sAPP $\alpha$  immunoneutralization
```

approaches prevented etazolate neuroprotection against A_B, indicating that etazolate exerts its neuroprotective effect via sAPP α induction. Our findings therefore indicate a relation between GABAA receptor signaling, the α -secretase pathway and neuroprotection, documenting a new therapeutic approach for AD treatment.

IT 51022-77-6, Etazolate
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (etazolate, neuroprotective drug linking GABAA receptor pharmacol. to amyloid precursor protein processing)
 RN 51022-77-6 CAPLUS
 CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid,
 1-ethyl-4-[2-(1-methylethylidene)hydrazinyl]-, ethyl ester (CA INDEX NAME)



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
 REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2008:493012 CAPLUS
 DOCUMENT NUMBER: 148:509885
 TITLE: Compositions and methods for treating neurological disorders or damage
 INVENTOR(S): Diamandis, Phedias; Tyers, Mike; Dirks, Peter B.
 PATENT ASSIGNEE(S): Can.
 SOURCE: Can. Pat. Appl., 3pp.
 CODEN: CPXXEB
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2606658	A1	20080413	CA 2007-2606658	20071012
US 20090076019	A1	20090319	US 2007-871562	20071012

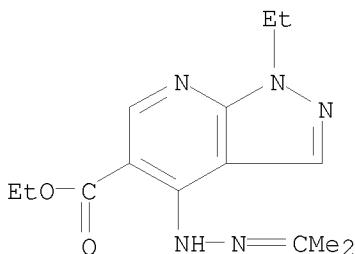
PRIORITY APPLN. INFO.: US 2006-851615P P 20061013
 AB The invention relates to a clonogenic neurosphere assay to carry out high throughput screens (HTS) to identify potent and/or selective modulators of proliferation, differentiation and/or renewal of neural precursor cells, neural progenitor cells and/or self-renewing and multipotent neural stem cells (NSCs). The invention also relates to compns. comprising the identified modulators and methods of using the modulators and compns., in particular to treat neurol. disorders (e.g. brain or CNS cancer) or damage.

IT 35838-58-5, Etazolate hydrochloride
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(screening for compns. and methods for treating neurol. disorders or damage with modulators of neural stem cells)

RN 35838-58-5 CAPLUS

CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid,
1-ethyl-4-[2-(1-methylethylidene)hydrazinyl]-, ethyl ester, hydrochloride
(1:1) (CA INDEX NAME)



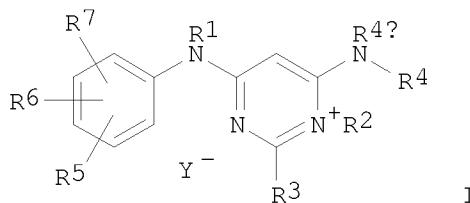
● HCl

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
(1 CITINGS)

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:874191 CAPLUS
DOCUMENT NUMBER: 147:227213
TITLE: Compositions and methods using pyrimidine-4,6-diamine derivative Ih (hyperpolarization-activated cationic current) channel blockers for treating cognitive disorders
INVENTOR(S): Arnsten, Amy F. T.; Wang, Min; McCormick, David A.; Ramos, Brian P.
PATENT ASSIGNEE(S): Yale University, USA
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

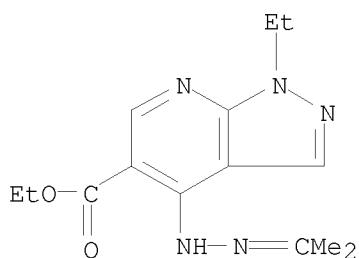
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007089774	A2	20070809	WO 2007-US2527	20070131
WO 2007089774	A3	20071115		
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EP 1993612	A2	20081126	EP 2007-762676	20070131
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL,				

BA, HR, MK, RS
 US 20090221610 A1 20090903 US 2008-86658 20081222
 PRIORITY APPLN. INFO.: US 2006-763802P P 20060131
 WO 2007-US2527 W 20070131
 OTHER SOURCE(S): MARPAT 147:227213
 GI



AB The invention discloses the use of inhibitors or blockers of Ih (hyperpolarization-activated cationic current) channels in the treatment of cognitive disorders. In preferred aspects of the invention, an effective amount of a compound I [R1 = H, (un)substituted C1-3 alkyl; R2 = (un)substituted C1-3 alkyl; R3 = H, (un)substituted C1-3 alkyl, halo, O(C1-3)alkyl; R4 = (un)substituted C1-6 alkyl, C(O)-(C1-5)alkyl, etc.; R4a = H, (un)substituted C1-6 alkyl; R5-R7 = H, halo, (un)substituted C1-6 alkyl, etc.; Y- = anion of pharmaceutically acceptable salt]; or a solvate or polymorph thereof, is administered to a patient, optionally, in combination with guanfacine and/or chelerythrine, and a pharmaceutically acceptable carrier, additive or excipient.

IT 51022-77-6, Etazolate
 RL: PAC (Pharmacological activity); BIOL (Biological study)
 (pyrimidinediamine derivative Ih channel blockers for treatment of cognitive disorders)
RN 51022-77-6 CAPLUS
CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid,
 1-ethyl-4-[2-(1-methylethylidene)hydrazinyl]-, ethyl ester (CA INDEX NAME)



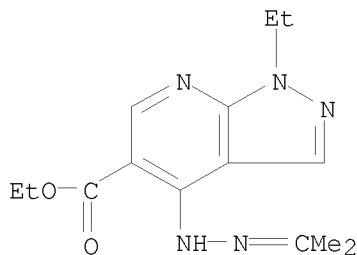
L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:216623 CAPLUS
DOCUMENT NUMBER: 142:274015
TITLE: Treatment or prevention of vascular disorders with cyclooxygenase 2 (COX-2) inhibitors in combination with cyclic AMP-specific phosphodiesterase inhibitors
INVENTOR(S): Taylor, Duncan P.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005020926	A2	20050310	WO 2004-US28118	20040827
WO 2005020926	A3	20050506		
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US 20050187278	A1	20050825	US 2004-927198	20040826
PRIORITY APPLN. INFO.:			US 2003-498529P	P 20030828
			US 2003-513099P	P 20031021
AB	A method is described for the prevention and/or treatment of vascular disorders and vascular disorder-related complications in a subject, the method comprising administering to the subject a COX-2 inhibitor in combination with a cAMP-specific PDE inhibitor. Also described are therapeutic and pharmaceutical compns. and kits that are useful in the invention. Preparation of celecoxib is also described.			
IT	35838-58-5, Etazolate hydrochloride RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (cyclooxygenase 2 inhibitor combination with cAMP-specific phosphodiesterase inhibitor for treatment or prevention of vascular disorder)			
RN	35838-58-5 CAPLUS			
CN	1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-ethyl-4-[2-(1-methylethylidene)hydrazinyl]-, ethyl ester, hydrochloride (1:1) (CA INDEX NAME)			



● HCl

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD
(3 CITINGS)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

DOCUMENT NUMBER: 142:86671
 TITLE: Methods and compositions for the treatment of cognitive deficiencies with ligands for the benzodiazepine peripheral receptor
 INVENTOR(S): Schweighoffer, Fabien; Desire, Laurent; Resink, Annelies
 PATENT ASSIGNEE(S): Exonhit Therapeutics S. A., Fr.
 SOURCE: Fr. Demande, 34 pp.
 CODEN: FRXXBL
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

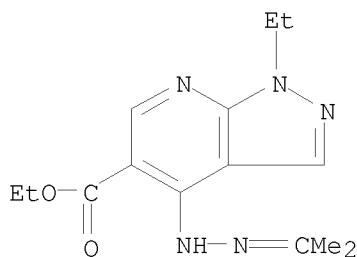
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2856595	A1	20041231	FR 2003-7824	20030627
FR 2856595	B1	20080530		
AU 2004251466	A1	20050106	AU 2004-251466	20040625
CA 2528284	A1	20050106	CA 2004-2528284	20040625
WO 2005000302	A1	20050106	WO 2004-FR1630	20040625
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1638559	A1	20060329	EP 2004-767477	20040625
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CN 1812786	A	20060802	CN 2004-80018148	20040625
JP 2007520427	T	20070726	JP 2006-516332	20040625
IN 2005DN05464	A	20070817	IN 2005-DN5464	20051128
US 20060142326	A1	20060629	US 2005-560774	20051214
PRIORITY APPLN. INFO.:			FR 2003-7824	A 20030627
			WO 2004-FR1630	W 20040625

AB The present invention relates to methods to improve, increase or facilitate the cognitive ability of subjects afflicted with neurodegenerative disorders. The invention more particularly involves ligands for the benzodiazepine peripheral receptor, preferably ligands of the pyrazolopyridine family, for the improvement of cognitive abilities in subjects afflicted with neurodegenerative disorders, particularly those with Alzheimer's disease.

IT 51022-77-6, Etazolate
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (as a ligand of the peripheral benzodiazepine receptor; methods and compns. for treatment of cognitive deficiencies with ligands for benzodiazepine peripheral receptor)

RN 51022-77-6 CAPLUS

CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid,
 1-ethyl-4-[2-(1-methylethylidene)hydrazinyl]-, ethyl ester (CA INDEX NAME)

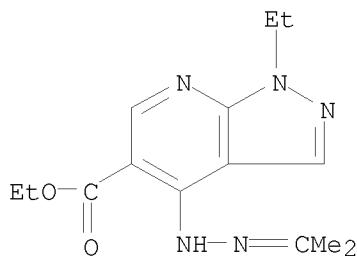


IT 35838-58-5, SQ 20009

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (methods and compns. for treatment of cognitive deficiencies with ligands for benzodiazepine peripheral receptor)

RN 35838-58-5 CAPLUS

CN 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid,
 1-ethyl-4-[2-(1-methylethylidene)hydrazinyl]-, ethyl ester, hydrochloride
 (1:1) (CA INDEX NAME)



● HCl

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
 (1 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:453015 CAPLUS

DOCUMENT NUMBER: 141:17632

TITLE: Methods and agents elevating cAMP and calcium ion for increasing neurogenesis

INVENTOR(S): Bertilsson, Goran; Erlandsson, Rikard; Friesen, Jonas;
 Haegestrand, Anders; Heidrich, Jessica; Hellstrom, Kristina; Hagblad, Johan; Jansson, Katarina;
 Kortesmaa, Jarkko; Lindquist, Per; Lundh, Hanna;
 McGuire, Jacqueline; Mercer, Alex; Njberg, Karl;
 Ossoinak, Amina; Patrone, Cesare; Ronnholm, Harriet;
 Zachrisson, Olof; Wikstrom, Lilian

PATENT ASSIGNEE(S): Neuronova AB, Swed.

SOURCE: PCT Int. Appl., 77 pp.

CODEN: PIXXD2

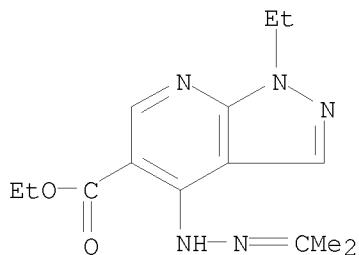
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004045592	A2	20040603	WO 2003-IB5311	20031120
WO 2004045592	A3	20041104		
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AU 2003280117	B2	20090910		
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JP 2006514630	T	20060511	JP 2004-553032	20031120
CA 2546843	A1	20050909	CA 2004-2546843	20041119
WO 2005081619	A2	20050909	WO 2004-IB4451	20041119
WO 2005081619	A3	20070419		
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EP 1750752	A2	20070214	EP 2004-821493	20041119
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PRIORITY APPLN. INFO.:				
		US 2002-427912P	P	20021120
		US 2003-718071	A	20031120
		WO 2003-IB5311	W	20031120
		US 2004-850055	A	20040519
		WO 2004-IB4451	W	20041119
AB	The invention discloses methods for promoting neurogenesis by contacting neuronal tissue with intracellular cAMP-elevating agents and intracellular calcium ion-elevating agents. Agents for promoting neurogenesis are also disclosed.			
IT	35838-58-5, Etazolatehydrochloride RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (cAMP-elevating and calcium ion-elevating compds. for increasing neurogenesis)			
RN	35838-58-5 CAPLUS			
CN	1H-Pyrazolo[3,4-b]pyridine-5-carboxylic acid, 1-ethyl-4-[2-(1-methylethylidene)hydrazinyl]-, ethyl ester, hydrochloride (1:1) (CA INDEX NAME)			



● HCl

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD
(8 CITINGS)

=> d his]
'HIS]' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'

The following are valid formats:

ABS ----- GI and AB
 ALL ----- BIB, AB, IND, RE
 APPS ----- AI, PRAI
 BIB ----- AN, plus Bibliographic Data and PI table (default)
 CAN ----- List of CA abstract numbers without answer numbers
 CBIB ----- AN, plus Compressed Bibliographic Data
 CLASS ----- IPC, NCL, ECLA, FTERM
 DALL ----- ALL, delimited (end of each field identified)
 DMAX ----- MAX, delimited for post-processing
 FAM ----- AN, PI and PRAI in table, plus Patent Family data
 FBIB ----- AN, BIB, plus Patent FAM
 IND ----- Indexing data
 IPC ----- International Patent Classifications
 MAX ----- ALL, plus Patent FAM, RE
 PATS ----- PI, SO
 SAM ----- CC, SX, TI, ST, IT
 SCAN ----- CC, SX, TI, ST, IT (random display, no answer numbers;
 SCAN must be entered on the same line as the DISPLAY,
 e.g., D SCAN or DISPLAY SCAN)
 STD ----- BIB, CLASS

 IABS ----- ABS, indented with text labels
 IALL ----- ALL, indented with text labels
 IBIB ----- BIB, indented with text labels
 IMAX ----- MAX, indented with text labels
 ISTD ----- STD, indented with text labels

 OBIB ----- AN, plus Bibliographic Data (original)
 OIBIB ----- OBIB, indented with text labels

 SBIB ----- BIB, no citations
 SIBIB ----- IBIB, no citations

 HIT ----- Fields containing hit terms
 HITIND ----- IC, ICA, ICI, NCL, CC and index field (ST and IT)
 containing hit terms
 HITRN ----- HIT RN and its text modification

HITSTR ----- HIT RN, its text modification, its CA index name, and its structure diagram
HITSEQ ----- HIT RN, its text modification, its CA index name, its structure diagram, plus NTE and SEQ fields
FHITSTR ----- First HIT RN, its text modification, its CA index name, and its structure diagram
FHITSEQ ----- First HIT RN, its text modification, its CA index name, its structure diagram, plus NTE and SEQ fields
KWIC ----- Hit term plus 20 words on either side
OCC ----- Number of occurrence of hit term and field in which it occurs

To display a particular field or fields, enter the display field codes. For a list of the display field codes, enter HELP DFIELDS at an arrow prompt (=>). Examples of formats include: TI; TI,AU; BIB,ST; TI,IND; TI,SO. You may specify the format fields in any order and the information will be displayed in the same order as the format specification.

All of the formats (except for SAM, SCAN, HIT, HITIND, HITRN, HITSTR, FHITSTR, HITSEQ, FHITSEQ, KWIC, and OCC) may be used with DISPLAY ACC to view a specified Accession Number.

ENTER DISPLAY FORMAT (BIB):
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'0' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'

The following are valid formats:

ABS ----- GI and AB
ALL ----- BIB, AB, IND, RE
APPS ----- AI, PRAI
BIB ----- AN, plus Bibliographic Data and PI table (default)
CAN ----- List of CA abstract numbers without answer numbers
CBIB ----- AN, plus Compressed Bibliographic Data
CLASS ----- IPC, NCL, ECLA, FTERM
DALL ----- ALL, delimited (end of each field identified)
DMAX ----- MAX, delimited for post-processing
FAM ----- AN, PI and PRAI in table, plus Patent Family data
FBIB ----- AN, BIB, plus Patent FAM
IND ----- Indexing data
IPC ----- International Patent Classifications
MAX ----- ALL, plus Patent FAM, RE
PAT5 ----- PI, SO
SAM ----- CC, SX, TI, ST, IT
SCAN ----- CC, SX, TI, ST, IT (random display, no answer numbers;
 SCAN must be entered on the same line as the DISPLAY,
 e.g., D SCAN or DISPLAY SCAN)
STD ----- BIB, CLASS

IABS ----- ABS, indented with text labels
IALL ----- ALL, indented with text labels
IBIB ----- BIB, indented with text labels
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ISTD ----- STD, indented with text labels

OBIB ----- AN, plus Bibliographic Data (original)
OIBIB ----- OBIB, indented with text labels

SBIB ----- BIB, no citations
SIBIB ----- IBIB, no citations

HIT ----- Fields containing hit terms
HITIND ----- IC, ICA, ICI, NCL, CC and index field (ST and IT)

containing hit terms

HITRN ----- HIT RN and its text modification
HITSTR ----- HIT RN, its text modification, its CA index name, and its structure diagram
HITSEQ ----- HIT RN, its text modification, its CA index name, its structure diagram, plus NTE and SEQ fields
FHITSTR ----- First HIT RN, its text modification, its CA index name, and its structure diagram
FHITSEQ ----- First HIT RN, its text modification, its CA index name, its structure diagram, plus NTE and SEQ fields
KWIC ----- Hit term plus 20 words on either side
OCC ----- Number of occurrence of hit term and field in which it occurs

To display a particular field or fields, enter the display field codes. For a list of the display field codes, enter HELP DFIELDS at an arrow prompt (=>). Examples of formats include: TI; TI,AU; BIB,ST; TI,IND; TI,SO. You may specify the format fields in any order and the information will be displayed in the same order as the format specification.

All of the formats (except for SAM, SCAN, HIT, HITIND, HITRN, HITSTR, FHITSTR, HITSEQ, FHITSEQ, KWIC, and OCC) may be used with DISPLAY ACC to view a specified Accession Number.

ENTER DISPLAY FORMAT (BIB):

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2008:827349 CAPLUS
DN 149:167804
TI Etazolate, a neuroprotective drug linking GABAA receptor pharmacology to amyloid precursor protein processing
AU Marcade, Maryline; Bourdin, Jerome; Loiseau, Nadia; Peillon, Helene; Rayer, Aurelie; Drouin, Dominique; Schweighoffer, Fabien; Desire, Laurent
CS Department of Neurology, ExonHit Therapeutics, Paris, Fr.
SO Journal of Neurochemistry (2008), 106(1), 392-404
CODEN: JONRA9; ISSN: 0022-3042
PB Blackwell Publishing Ltd.
DT Journal
LA English
OSC.G 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L1 STRUCTURE uploaded
L2 28 S L1 FULL

FILE 'CAPLUS' ENTERED AT 23:11:38 ON 11 OCT 2009
L3 167 S L2
L4 6 S L3 AND COGNITION

=> s l3 and alzheimer
59100 ALZHEIMER
L5 7 L3 AND ALZHEIMER

=> d 14 or 15
L5 IS NOT VALID HERE
For an explanation, enter "HELP DISPLAY".

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L5 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2008:827349 CAPLUS
DN 149:167804
TI Etazolate, a neuroprotective drug linking GABAA receptor pharmacology to amyloid precursor protein processing
AU Marcade, Maryline; Bourdin, Jerome; Loiseau, Nadia; Peillon, Helene; Rayer, Aurelie; Drouin, Dominique; Schweighoffer, Fabien; Desire, Laurent
CS Department of Neurology, ExonHit Therapeutics, Paris, Fr.
SO Journal of Neurochemistry (2008), 106(1), 392-404
CODEN: JONRA9; ISSN: 0022-3042
PB Blackwell Publishing Ltd.
DT Journal
LA English
OSC.G 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2008:91629 CAPLUS
DN 148:136029
TI Methods and tools for the therapy of neurodegenerative pathologies
IN Schweighoffer, Fabien; Desire, Laurent; Bourdin, Jerome
PA Exonhit Therapeutics SA, Fr.
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2008009868	A2	20080124	WO 2007-FR51706	20070720
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	FR 2904113	A1	20080125	FR 2006-6698	20060721
	AU 2007274872	A1	20080124	AU 2007-274872	20070720
	CA 2658464	A1	20080124	CA 2007-2658464	20070720
	EP 2047277	A2	20090415	EP 2007-823624	20070720
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	KR 2009086386	A	20090812	KR 2009-703519	20070720
	IN 2009CN00978	A	20090821	IN 2009-CN978	20090220
	CN 101542289	A	20090923	CN 2007-80034007	20090313
PRAI	FR 2006-6698	A	20060721		
	WO 2007-FR51706	W	20070720		

L5 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2005:588 CAPLUS

DN 142:86671
 TI Methods and compositions for the treatment of cognitive deficiencies with ligands for the benzodiazepine peripheral receptor
 IN Schweighoffer, Fabien; Desire, Laurent; Resink, Annelies
 PA Exonhit Therapeutics S. A., Fr.
 SO Fr. Demande, 34 pp.
 CODEN: FRXXBL

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2856595	A1	20041231	FR 2003-7824	20030627
	FR 2856595	B1	20080530		
	AU 2004251466	A1	20050106	AU 2004-251466	20040625
	CA 2528284	A1	20050106	CA 2004-2528284	20040625
	WO 2005000302	A1	20050106	WO 2004-FR1630	20040625
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	EP 1638559	A1	20060329	EP 2004-767477	20040625
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	CN 1812786	A	20060802	CN 2004-80018148	20040625
	JP 2007520427	T	20070726	JP 2006-516332	20040625
	IN 2005DN05464	A	20070817	IN 2005-DN5464	20051128
	US 20060142326	A1	20060629	US 2005-560774	20051214
PRAI	FR 2003-7824	A	20030627		
	WO 2004-FR1630	W	20040625		

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OSC.G 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN
 AN 2004:934227 CAPLUS
 DN 141:388737
 TI Phosphodiesterase 4B gene mutations in diagnosis of brain disorders and PDE4B inhibitors for treatment of brain disorders
 IN Ait, Ikhlef Ali; Resink, Annelies; Schweighoffer, Fabien
 PA Fr.
 SO U.S. Pat. Appl. Publ., 36 pp., Cont.-in-part of U.S. Ser. No. 983,754.
 CODEN: USXXCO

DT Patent

LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 20040219552	A1	20041104	US 2004-486639	20040212
	FR 2828693	A1	20030221	FR 2001-10819	20010814
	FR 2828693	B1	20040618		
	US 20030064374	A1	20030403	US 2001-983754	20011025
	US 6855736	B2	20050215		
	WO 2003016563	A2	20030227	WO 2002-FR2861	20020813

WO 2003016563	A3	20040401		
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EP 1982704	A2	20081022	EP 2008-160783	20020813
EP 1982704	A3	20081217		
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US 20050043319	A1	20050224	US 2004-857455	20040601
PRAI FR 2001-10819	A	20010814		
US 2001-983754	A2	20011025		
WO 2002-FR2861	W	20020813		
EP 2002-777405	A3	20020813		
US 2004-486639	A2	20040212		

OSC.G 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

L5 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2004:453015 CAPLUS
DN 141:17632
TI Methods and agents elevating cAMP and calcium ion for increasing neurogenesis
IN Bertilsson, Goran; Erlandsson, Rikard; Frisen, Jonas; Haegestrand, Anders; Heidrich, Jessica; Hellstrom, Kristina; Haggblad, Johan; Jansson, Katarina; Kortesmaa, Jarkko; Lindquist, Per; Lundh, Hanna; McGuire, Jacqueline; Mercer, Alex; Njberg, Karl; Ossoinak, Amina; Patrone, Cesare; Ronholm, Harriet; Zachrisson, Olof; Wikstrom, Lilian
PA Neuronova AB, Swed.
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004045592	A2	20040603	WO 2003-IB5311	20031120
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	CA 2506850	A1	20040603	CA 2003-2506850	20031120
	AU 2003280117	A1	20040615	AU 2003-280117	20031120
	AU 2003280117	B2	20090910		
	EP 1583541	A2	20051012	EP 2003-772495	20031120
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	JP 2006514630	T	20060511	JP 2004-553032	20031120
	CA 2546843	A1	20050909	CA 2004-2546843	20041119
	WO 2005081619	A2	20050909	WO 2004-IB4451	20041119

WO 2005081619	A3	20070419		
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EP 1750752	A2	20070214	EP 2004-821493	20041119
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, HR, LT, LV, MK, YU			
PRAI US 2002-427912P	P	20021120		
US 2003-718071	A	20031120		
WO 2003-IB5311	W	20031120		
US 2004-850055	A	20040519		
WO 2004-IB4451	W	20041119		

OSC.G 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)

L5	ANSWER 6 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN			
AN	2003:154633 CAPLUS			
DN	138:203092			
TI	A gene for a phosphodiesterase isoenzyme playing a role in excitotoxicity in the etiology of neurodegenerative disease			
IN	Aiet Ikhlef, Ali; Resink, Annelies; Schweighoffer, Fabien			
PA	Exonhit Therapeutics S.A., Fr.			
SO	PCT Int. Appl., 64 pp. CODEN: PIXXD2			
DT	Patent			
LA	French			
FAN.CNT	3			
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2003016563	A2	20030227	WO 2002-FR2861	20020813
WO 2003016563	A3	20040401		
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FR 2828693	B1	20040618		
CA 2457611	A1	20030227	CA 2002-2457611	20020813
AU 2002339017	A1	20030303	AU 2002-339017	20020813
AU 2002339017	B2	20071101		
EP 1417349	A2	20040512	EP 2002-777405	20020813
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CN 1541278	A	20041027	CN 2002-815840	20020813
JP 2005500066	T	20050106	JP 2003-521870	20020813
NZ 530939	A	20061130	NZ 2002-530939	20020813
EP 1982704	A2	20081022	EP 2008-160783	20020813

EP 1982704 A3 20081217
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT,
LI, LU, MC, NL, PT, SE, SK, TR
AT 414790 T 20081215 AT 2002-777405 20020813
ES 2316625 T3 20090416 ES 2002-777405 20020813
US 20040219552 A1 20041104 US 2004-486639 20040212
US 20050043319 A1 20050224 US 2004-857455 20040601
PRAI FR 2001-10819 A 20010814
US 2001-983754 A2 20011025
EP 2002-777405 A3 20020813
WO 2002-FR2861 W 20020813
US 2004-486639 A2 20040212

OSC.G 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2000:62023 CAPLUS
DN 132:216984
TI Interaction of various intracellular signaling mechanisms involved in mononuclear phagocyte toxicity toward neuronal cells
AU Klegeris, Andis; McGeer, Patrick L.
CS Kinsmen Laboratory of Neurological Research, University of British Columbia, Vancouver, BC, V6T 1Z3, Can.
SO Journal of Leukocyte Biology (2000), 67(1), 127-133
CODEN: JLBIE7; ISSN: 0741-5400
PB Federation of American Societies for Experimental Biology
DT Journal
LA English
OSC.G 32 THERE ARE 32 CAPLUS RECORDS THAT CITE THIS RECORD (32 CITINGS)
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>
=> s pde4
L6 1720 PDE4

=> s 16 and alzheimer and cognition
59100 ALZHEIMER
19561 COGNITION
L7 51 L6 AND ALZHEIMER AND COGNITION

=> s pde4b
L8 287 PDE4B

=> s 18 and alzheimer and cognition
59100 ALZHEIMER
19561 COGNITION
L9 0 L8 AND ALZHEIMER AND COGNITION

=> d 17 30-51 ibib abs

L7 ANSWER 30 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:380892 CAPLUS
DOCUMENT NUMBER: 144:432795
TITLE: Preparation of pyrazole derivatives as selective phosphodiesterase 4 inhibitors
INVENTOR(S): Hopper, Allen; Dunn, Robert F.; Kuester, Erik Mikal;
Conticello, Richard D.
PATENT ASSIGNEE(S): Memory Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 221 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

1

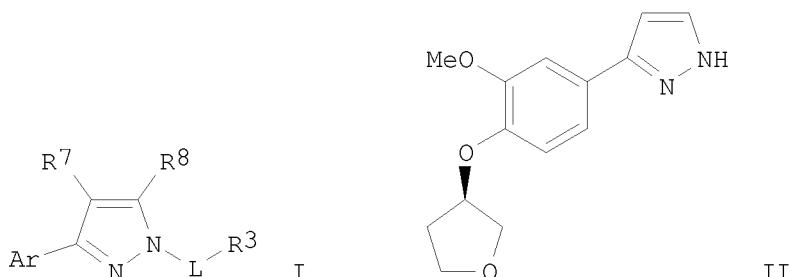
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006044528	A1	20060427	WO 2005-US36801	20051014
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005295753	A1	20060427	AU 2005-295753	20051014
CA 2584317	A1	20060427	CA 2005-2584317	20051014
US 20060154960	A1	20060713	US 2005-249769	20051014
US 7432266	B2	20081007		
EP 1799673	A1	20070627	EP 2005-816308	20051014
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
JP 2008516964	T	20080522	JP 2007-536876	20051014
CN 101166733	A	20080423	CN 2005-80043196	20070615
US 20080207660	A1	20080828	US 2008-108833	20080424
PRIORITY APPLN. INFO.:			US 2004-618725P	P 20041015
			US 2005-249769	A3 20051014
			WO 2005-US36801	W 20051014

OTHER SOURCE(S):

MARPAT 144:432795

GI



AB Title (hetero)aryl pyrazole compds. I [wherein Ar = substituted Ph, pyridinyl, benzo-furanyl, benzo-pyrazolyl, pyrazolo[4,3-b]pyridinyl; L = bond, (CH₂)_nCONH, (CH₂)_nCON(alkyl), (CH₂)_nNHCO, (CH₂)_nCONHSO₂, (CH₂)_nSO₂NH, (CH₂)_nSO₂, (CH₂)_nCO₂, (un)substituted alkylene optionally interrupted by O, NH, S; n = 0-3; R₃ = H, (un)substituted (cyclo)alkyl, alkenyl, alkynyl, aryl, heterocyclyl; R₇, R₈ = independently H, halo, (un)substituted alkyl, alkenyl, alkynyl; and pharmaceutically acceptable salts thereof] were prepared. The invention compds. exhibited improved phosphodiesterase 4 (PDE4) inhibition as compared to compds. such as rolipram and showed selectivity with regard to inhibition of other

classes of PDEs. For example, 3-hydroxy-4-methoxy-benzaldehyde was condensed with (S)-3-hydroxy-tetrahydrofuran using PPh₃ and DIAD in THF to give (R)-4-methoxy-3-[(tetrahydrofuran-3-yl)oxy]benzaldehyde (66%). Reaction of the aldehyde with diethoxyphosphorylacetalddehyde tosyl-hydrazone in the presence of NaH in THF provided the desired pyrazole II (57%). Compds. of the invention blocked the human PDE4 mediated conversion of cAMP to adenosine with IC₅₀ values ranging from 10 nM to 5000 nM. Thus, I and their pharmaceutical compns. are useful for enhancing cognition and treating psychosis, allergic conditions, or inflammatory disease, Alzheimer's disease, schizophrenia, Parkinson's disease, Huntington's disease, Pick's disease, Cretzfeldt-Jakob disease, HIV, cardiovascular disease, head trauma or age-related cognitive decline, schizophrenia, bipolar or manic depression, major depression, drug addiction or morphine dependence (no data).

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
(1 CITINGS)
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 31 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:1018151 CAPLUS
DOCUMENT NUMBER: 143:278260
TITLE: Phosphodiesterase inhibitors for cognitive enhancement
AUTHOR(S): Rose, Gregory M.; Hopper, Allen; De Vivo, Michael;
Tehim, Ashok
CORPORATE SOURCE: Memory Pharmaceuticals Corp., Montvale, NJ, 07645, USA
SOURCE: Current Pharmaceutical Design (2005), 11(26),
3329-3334
CODEN: CPDEFP; ISSN: 1381-6128
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. An effective treatment for age-related cognitive deficits remains an unmet medical need. Currently available drugs for the symptomatic treatment of Alzheimer's disease or other dementias have limited efficacy. This may be due to their action at only one of the many neurotransmitter systems involved in the complex mechanisms that underlie cognition. An alternative approach would be to target second messenger systems that are utilized by multiple neurotransmitters. cAMP is a second messenger that plays a key role in biochem. processes that regulate the cognitive process of memory consolidation. Prolongation of cAMP signals can be accomplished by inhibiting phosphodiesterases (PDEs). Eleven PDE families, comprised of more than 50 distinct members, are currently known. This review summarizes the evidence demonstrating that rolipram, a selective inhibitor of cAMP-selective PDE4 enzymes, has pos. effects on learning and memory in animal models. These data provide support for the general approach of second messenger modulation as a potential therapy for cognitive dysfunction, and specifically suggest that PDE4 inhibitors may have utility for improving the symptoms of cognitive decline associated with neurodegenerative and psychiatric diseases.

OS.CITING REF COUNT: 40 THERE ARE 40 CAPLUS RECORDS THAT CITE THIS RECORD (40 CITINGS)
REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 32 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:965063 CAPLUS
DOCUMENT NUMBER: 141:410960
TITLE: Preparation of 8-(3-biaryl)phenylquinoline phosphodiesterase-4 inhibitors

INVENTOR(S): Dube, Daniel; Dube, Laurence; Gallant, Michel;
 Lacombe, Patrick; Deschenes, Denis; MacDonald, Dwight
 PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
 SOURCE: PCT Int. Appl., 129 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096220	A1	20041111	WO 2004-CA622	20040427
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004234190	A1	20041111	AU 2004-234190	20040427
CA 2523336	A1	20041111	CA 2004-2523336	20040427
EP 1635829	A1	20060322	EP 2004-729586	20040427
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1812787	A	20060802	CN 2004-80018346	20040427
CN 100441185	C	20081210		
JP 2006524638	T	20061102	JP 2006-504121	20040427
US 20060223850	A1	20061005	US 2005-554176	20051021
US 7482456	B2	20090127		
IN 2005DN04934	A	20070928	IN 2005-DN4934	20051027
PRIORITY APPLN. INFO.:			US 2003-466542P	P 20030430
			WO 2004-CA622	W 20040427

OTHER SOURCE(S): MARPAT 141:410960
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title 8-phenylquinolines I [S1-S3 = H, OH, halo, alkyl, etc.; R1 = CO₂aryl, CONHaryl, CONHeteroaryl, etc.; Ar₁, Ar₂ = (hetero)aryl or an N-oxide thereof; R₂ = H, aryl, haloaryl, heterocyclyl, etc.; R₃ = H, alkyl, hydroxyalkyl, etc.; R₄ = H, halo, CN, alkyl, etc.] which are PDE4 inhibitors, were prepared E.g., a multi-step synthesis of II (no characterization data given for intermediates), which showed IC₅₀ of 0.155 μM in LPS and FMLP-induced TNF-α and LTB₄ assays in human whole blood, was given. The pharmaceutical compns. comprising the compound I are claimed.

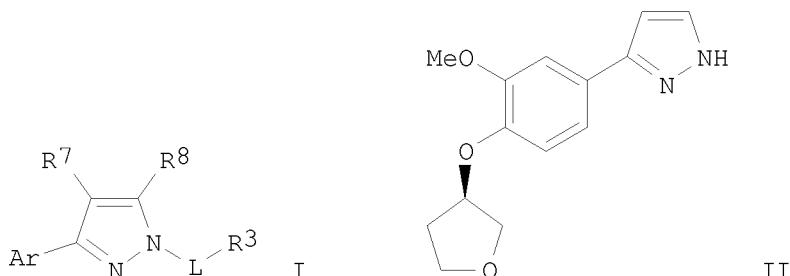
OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD
 (2 CITINGS)
 REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 33 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2004:927199 CAPLUS
 DOCUMENT NUMBER: 141:379922

TITLE: Preparation of pyrazole derivatives as selective phosphodiesterase 4 inhibitors
 INVENTOR(S): Hopper, Allen; Kuester, Erik; Dunn, Robert;
 Conticello, Richard
 PATENT ASSIGNEE(S): Memory Pharmaceuticals Corporation, USA
 SOURCE: PCT Int. Appl., 186 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004094411	A1	20041104	WO 2004-US11899	20040416
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004232973	A1	20041104	AU 2004-232973	20040416
CA 2522687	A1	20041104	CA 2004-2522687	20040416
US 20040229918	A1	20041118	US 2004-825611	20040416
US 7226930	B2	20070605		
EP 1631568	A1	20060308	EP 2004-759965	20040416
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
BR 2004009888	A	20060523	BR 2004-9888	20040416
CN 1809559	A	20060726	CN 2004-80017033	20040416
JP 2006523719	T	20061019	JP 2006-513094	20040416
MX 2005011200	A	20051214	MX 2005-11200	20051018
IN 2005DN04777	A	20070817	IN 2005-DN4777	20051019
US 20070203197	A1	20070830	US 2007-797151	20070501
US 7495017	B2	20090224		
US 20090221661	A1	20090903	US 2009-389873	20090220
PRIORITY APPLN. INFO.:			US 2003-463725P	P 20030418
			US 2004-825611	A3 20040416
			WO 2004-US11899	W 20040416
			US 2007-797151	A1 20070501

OTHER SOURCE(S): MARPAT 141:379922
 GI



AB Title (hetero)aryl pyrazole compds. I [wherein Ar = substituted Ph, pyridinyl, benzofuranyl, benzopyrazolyl, pyrazolo[4,3-b]pyridinyl; L = bond, (CH₂)_nCONH, (CH₂)_nCON(alkyl), (CH₂)_nNHCO, (CH₂)_nCONHSO₂, (CH₂)_nSO₂NH, (CH₂)_nSO₂, (CH₂)_nCO₂, (un)substituted alkylene optionally interrupted by O, NH, S; n = 0-3; R₃ = H, (un)substituted (cyclo)alkyl, alkenyl, alkynyl, aryl, heterocyclyl; R₇, R₈ = independently H, halo, (un)substituted alkyl, alkenyl, alkynyl; and pharmaceutically acceptable salts thereof] were prepared. The invention compds. exhibited improved phosphodiesterase 4 (PDE4) inhibition as compared to compds. such as rolipram and showed selectivity with regard to inhibition of other classes of PDEs. For example, 3-hydroxy-4-methoxybenzaldehyde was condensed with (S)-3-hydroxytetrahydrofuran using PPh₃ and DIAD in THF to give (R)-4-methoxy-3-[(tetrahydrofuran-3-yl)oxy]benzaldehyde (66%). Reaction of the aldehyde with diethoxyphosphorylacetaldehyde tosylhydrazone in the presence of NaH in THF provided the desired pyrazole II (57%). Compds. of the invention blocked the human PDE4 mediated conversion of cAMP to adenosine with IC₅₀ values ranging from 10 nM to 5000 nM. Thus, I and their pharmaceutical compns. are useful for enhancing cognition and treating psychosis, allergic conditions, or inflammatory disease (no data).

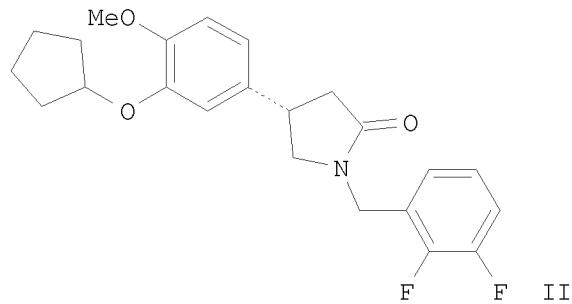
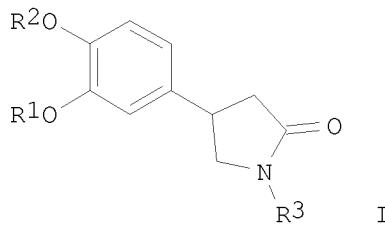
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
(1 CITINGS)
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 34 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:927168 CAPLUS
DOCUMENT NUMBER: 141:395413
TITLE: Preparation of 4-(substituted-phenyl)-2-pyrrolidinone derivatives as selective phosphodiesterase 4 inhibitors
INVENTOR(S): Tehim, Ashok; Hopper, Allen; Liu, Ruiping; Kuester, Erik; Dunn, Robert F.; Renau, Thomas E.
PATENT ASSIGNEE(S): Memory Pharmaceuticals Corporation, USA; Hoffmann La-Roche Inc.
SOURCE: PCT Int. Appl., 195 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004094375	A2	20041104	WO 2004-US11765	20040416
WO 2004094375	A3	20050421		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004232958	A1	20041104	AU 2004-232958	20040416
CA 2522631	A1	20041104	CA 2004-2522631	20040416
US 20050026913	A1	20050203	US 2004-825610	20040416

EP 1613590	A2	20060111	EP 2004-750220	20040416
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
BR 2004010235	A	20060509	BR 2004-10235	20040416
CN 1805929	A	20060719	CN 2004-80016778	20040416
JP 2006523710	T	20061019	JP 2006-510117	20040416
MX 2005011055	A	20061207	MX 2005-11055	20051014
KR 2006039392	A	20060508	KR 2005-719778	20051017
IN 2005DN04695	A	20070928	IN 2005-DN4695	20051017
PRIORITY APPLN. INFO.:			US 2003-463054P	P 20030416
			WO 2004-US11765	W 20040416

OTHER SOURCE(S): MARPAT 141:395413
GI



AB Title pyrrolidinones compds. I [R1 = alkyl, wherein optionally 1 or more CH₂CH₂ groups are replaced by CH:CH or C.tplbond.C, (un)substituted cycloalkyl, aryl, arylalkyl, arylalkenyl, (un)saturated heterocyclyl, heterocyclylalkyl, etc.; R2 = (un)substituted alkyl; R3 = C(:O)R4; CH₂CO₂R₅, (CH₂)_nSR₅, etc.; R4 = (un)substituted alkoxyalkyl, cycloalkyl, aryl, arylalkyl, etc.; R5 = H, (un)substituted alkoxy/alkyl, cycloalkyl, aryl, etc.] were prepared. The invention compds. exhibited improved phosphodiesterase 4 (PDE4) inhibition as compared to compds. such as rolipram and showed selectivity with regard to inhibition of other classes of PDEs. For example, reacting 4-(3-cyclopentyloxy-4-methoxyphenyl)-2-pyrrolidinone with 2,3-difluorobenzyl bromide gave II in 70% yield. Selected I blocked the human PDE4 mediated conversion of cAMP to adenosine with IC₅₀ values < 10 nM. Thus, I and their pharmaceutical compns. are useful for enhancing cognition and treating psychosis, allergic conditions, or inflammatory disease (no data).

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
(1 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 35 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:857402 CAPLUS
DOCUMENT NUMBER: 141:325764
TITLE: Growth hormone secretagogue-phosphodiesterase 4 inhibitor combination for the treatment of Alzheimer's disease
INVENTOR(S): Castro Pineiro, Jose Luis
PATENT ASSIGNEE(S): Merck Sharp & Dohme Limited, UK
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004087157	A2	20041014	WO 2004-GB1435	20040401
WO 2004087157	A3	20041118		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004226698	A1	20041014	AU 2004-226698	20040401
CA 2521046	A1	20041014	CA 2004-2521046	20040401
CN 1764457	A	20060426	CN 2004-80008035	20040401
EP 1660086	A2	20060531	EP 2004-725099	20040401
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
JP 2006522084	T	20060928	JP 2006-506077	20040401
US 20060183764	A1	20060817	US 2005-552367	20051003
IN 2005DN04491	A	20071012	IN 2005-DN4491	20051004
PRIORITY APPLN. INFO.:			GB 2003-7863	A 20030404
			WO 2004-GB1435	A 20040401

AB The invention discloses the treatment or prevention of diseases involving deposition of β -amyloid in the brain, e.g. Alzheimer's disease, via the combined administration of a growth hormone secretagogue and a PDE4 inhibitor.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
(1 CITINGS)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 36 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:756612 CAPLUS
DOCUMENT NUMBER: 141:277367
TITLE: Preparation of diphenylethylene compounds as PDE4 inhibitors for treatment of cancer, CNS disorders, and inflammatory disorders
INVENTOR(S): Muller, George W.; Payvandi, Faribourz; Zhang, Ling H.; Robarge, Michael J.; Chen, Roger; Man, Hon-Wah
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 218 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

2

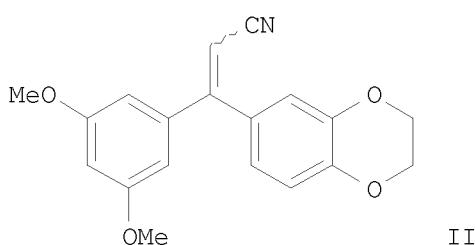
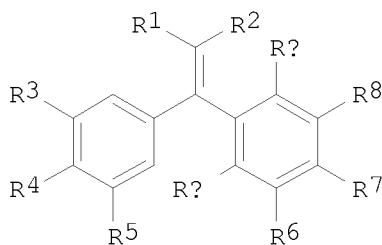
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004078144	A2	20040916	WO 2004-US6781	20040305
WO 2004078144	A3	20041209		
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AU 2004218364	A1	20040916	AU 2004-218364	20040305
CA 2517886	A1	20040916	CA 2004-2517886	20040305
EP 1603864	A2	20051214	EP 2004-718007	20040305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
BR 2004008005	A	20060214	BR 2004-8005	20040305
CN 1780811	A	20060531	CN 2004-80011822	20040305
JP 2006519874	T	20060831	JP 2006-509173	20040305
ZA 2005007321	A	20070328	ZA 2005-7321	20040305
CN 101053558	A	20071017	CN 2007-10101369	20040305
NZ 542407	A	20080829	NZ 2004-542407	20040305
PRIORITY APPLN. INFO.:			US 2003-452460P	P 20030305
			CN 2004-80011822	A3 20040305
			WO 2004-US6781	A 20040305

OTHER SOURCE(S):

MARPAT 141:277367

GI



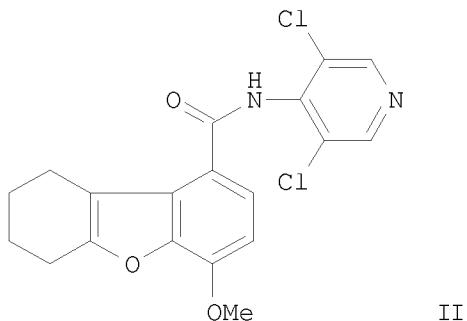
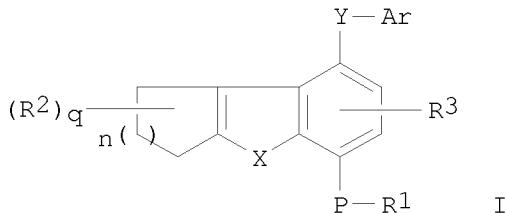
AB The invention relates to the preparation of title compds. I [wherein R1, R2 = independently H, CN, alkoxy(carbonyl), alkanoyl, carbamoyl, (un)substituted alkyl, alkenyl, alkynyl, aryl, heterocyclyl; Rc, Rd, R6-R8 = independently H, halo, CN, NO₂, OH, (un)substituted (cyclo)alkyl, aryl, heterocyclyl, alkoxy, amino, carboxy, carbamoyl, ureido, etc.; R3-R5 = independently halo, CN, NO₂, OH, (un)substituted (cyclo)alkyl, aryl, heterocyclyl, alkoxy, amino, carboxy, carbamoyl, ureido, etc.; and pharmaceutically acceptable salts, solvates, or hydrates thereof] as phosphodiesterase IV (PDE4) inhibitors (no data). For example, reductive addition of 6-bromo-2,3-dihydrobenzo[1,4]dioxin with 3,5-dimethoxybenzaldehyde gave (2,3-dihydrobenzo[1,4]dioxin-6-yl)(3,5-dimethoxyphenyl)methanol (91%), which was oxidized using activated MnO₂ powder to the methanone (93%). Reaction of the methanone with cyanomethylphosphonic acid di-Et ester in the presence of lithium

bis(trimethylsilyl)amide provided II (88%). The present invention also relates to methods for preventing or treating cancer, a CNS disorder, or an inflammatory disorder by administering one or more diphenylethylene compds. I optionally in combination with one or more other therapeutical agents. The present invention further relates to articles of manufacture and kits comprising I.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD
(3 CITINGS)

L7 ANSWER 37 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:675744 CAPLUS
DOCUMENT NUMBER: 141:207059
TITLE: Tricyclic compounds (dibenzofurans, dibenzothiophenes, carbazoles, and analogs) with PDE4 inhibitory activity, useful for the treatment of inflammatory and allergic disorders, process for their preparation, and methods of use
INVENTOR(S): Balasubramanian, Gopalan; Gharat, Laxmikant Atmaram; Lakdawala, Aftab Dawoodbhai; Bedekar, Sarika Suhas
PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Ltd., India
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004069831	A1	20040819	WO 2004-IB330	20040210
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
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IN 2003MU00177	A	20050204	IN 2003-MU177	20030210
PRIORITY APPLN. INFO.:			IN 2003-MU177	A 20030210
OTHER SOURCE(S):	MARPAT	141:207059		
GI				



AB The invention relates to novel heterocyclic compds. and their analogs, tautomers, regioisomers, stereoisomers, enantiomers, diastereomers, polymorphs, pharmaceutically acceptable salts, appropriate oxides, and pharmaceutically acceptable solvates, as well as pharmaceutical compns. containing them. The invention more particularly relates to novel phosphodiesterase type 4 (PDE4) inhibitors. In particular, compds. I and their aforementioned related compds. are claimed [wherein: R1, R2, R3 = H, (un)substituted alk(en/yn)yl, cycloalk(en)yl, cycloalkylalkyl, (hetero)aryl(alkyl), heterocyclyl(alkyl), COR1, COOR1, CONR1R1, S(O)mR1, S(O)mNR1R1, NO2, OH, cyano, amino, formyl, acetyl, halo, OR1, SR1, protecting groups, or two ortho R2 may form 3- to 7-membered ring with 0-2 optional NR1/O/S heteroatoms; X = O, S(O)m, NH, or NR5; Y = CONR4, NR4SO2, SO2NR4, and NR4CO; P = O or S; q = 0-5; n = 1-3; m = 0-2; Ar = (un)substituted aryl, arylalkyl, heterocyclic, or heteroaryl; R4 = H, (un)substituted alkyl, OH, OR1, aryl, or heterocyclic; R5 = (un)substituted alk(en/yn)yl, cycloalk(en)yl, cycloalkylalkyl, (hetero)aryl, (hetero)arylalkyl, heterocyclyl(alkyl), COR1, COOR1, CONR1R1, S(O)mR1, S(O)mNR1R1, NO2, OH, cyano, amino, formyl, acetyl, halo, OR1, SR1, and protecting groups]. The compds. (33 examples) were prepared and tested for PDE4 inhibitory activity. For instance, 6-methoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-carboxylic acid chloride [prepared in 5 steps from 2-methoxyphenol (guaicol) and 2-bromocyclohexanone] was amidated with 4-amino-3,5-dichloropyridine in DMF/THF to give invention compound II. This compound had an IC50 value of 0.4468 nM against PDE4 in vitro.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD
(4 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 38 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:467889 CAPLUS

DOCUMENT NUMBER: 141:38596

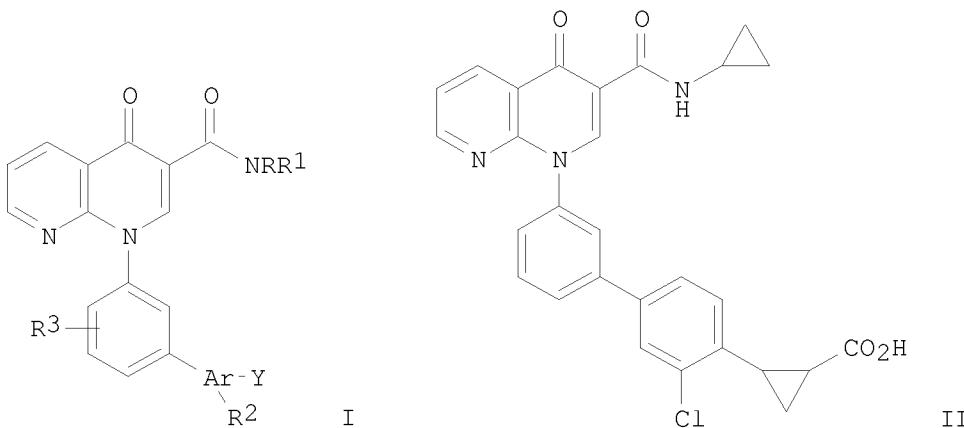
TITLE: Preparation of biphenylnaphthyridonecarboxamides as phosphodiesterase-4 inhibitors

INVENTOR(S): Dube, Daniel; Gallant, Michel; Lacombe, Patrick; Aspiotis, Renee; Dube, Laurence; Girard, Yves;

PATENT ASSIGNEE(S): MacDonald, Dwight
 SOURCE: Merck Frosst Canada & Co., Can.
 DOCUMENT TYPE: PCT Int. Appl., 116 pp.
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004048374	A1	20040610	WO 2003-CA1800	20031119
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CA 2506648	A1	20040610	CA 2003-2506648	20031119
AU 2003283167	A1	20040618	AU 2003-283167	20031119
AU 2003283167	B2	20090108		
EP 1565464	A1	20050824	EP 2003-775029	20031119
EP 1565464	B1	20080723		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003016458	A	20051011	BR 2003-16458	20031119
CN 1738819	A	20060222	CN 2003-80108952	20031119
CN 100475813	C	20090408		
JP 2006508989	T	20060316	JP 2004-554102	20031119
RU 2312865	C2	20071220	RU 2005-119644	20031119
NZ 539812	A	20071221	NZ 2003-539812	20031119
AT 402175	T	20080815	AT 2003-775029	20031119
US 20050107402	A1	20050519	US 2004-764229	20040123
US 7238706	B2	20070703		
ZA 2005003586	A	20060726	ZA 2005-3586	20050505
US 20060058316	A1	20060316	US 2005-534582	20050511
US 7342024	B2	20080311		
MX 2005005413	A	20050803	MX 2005-5413	20050520
NO 2005003046	A	20050727	NO 2005-3046	20050621
PRIORITY APPLN. INFO.:			US 2002-428611P	P 20021122
			WO 2003-CA1800	W 20031119

OTHER SOURCE(S): MARPAT 141:38596
 GI



AB Title compds. [I; Ar = Ph, pyridyl, pyrimidyl, indolyl, quinolyl, thienyl, pyridonyl, oxazolyl, oxadiazolyl, thiadiazolyl, imidazolyl; Y = CO₂R₄, ACO₂R₄, etc.; A = alkyl; R, R₄ = H, alkyl; R₁ = H, (substituted) alkyl, cycloalkyl, alkoxy, alkenyl, alkynyl, heteroaryl, heterocyclyl; R₂ = H, halo, cyano, NO₂, (substituted) alkyl, cycloalkyl, alkoxy, Ph, heteroaryl, amino, etc.; R₃ = H, halo, cyano, NO₂, (substituted) alkyl, cycloalkyl, etc.], were prepared. Thus, title compound (II) (preparation outlined) inhibited

PDE4-mediated hydrolysis of cAMP to AMP with IC₅₀ = 0.1 nM.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
(1 CITINGS)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 39 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:143155 CAPLUS

DOCUMENT NUMBER: 140:199339

TITLE: Preparation of 6-aminopurines and related compounds as selective phosphodiesterase-4 inhibitors for treatment of psychosis and inflammation

INVENTOR(S): Liu, Ruiping; Hopper, Allen T.; Tehim, Ashok; Hess, Hans-Jurgen E.; Rong, Yajing

PATENT ASSIGNEE(S): Memory Pharmaceuticals Corporation, USA

SOURCE: PCT Int. Appl., 125 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

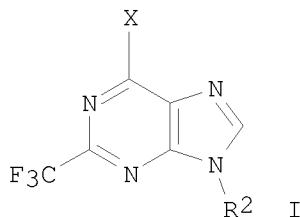
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014913	A2	20040219	WO 2003-US24914	20030808
WO 2004014913	A3	20040729		
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BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 CA 2494028 A1 20040219 CA 2003-2494028 20030808
 AU 2003264017 A1 20040225 AU 2003-264017 20030808
 EP 1529049 A2 20050511 EP 2003-785075 20030808
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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 CN 1688580 A 20051026 CN 2003-823977 20030808
 JP 2005538134 T 20051215 JP 2004-527913 20030808
 US 20070093510 A1 20070426 US 2003-636979 20030808
 US 7332486 B2 20080219
 US 20080139583 A1 20080612 US 2008-26198 20080205
 PRIORITY APPLN. INFO.: US 2002-401765P P 20020808
 OTHER SOURCE(S): MARPAT 140:199339
 GI US 2003-636979 A1 20030808
 WO 2003-US24914 W 20030808



AB Title compds. I [X = NHR1; R1 = H, (un)substituted alkyl, cycloalkyl, etc.; R2 = (un)substituted aryl, heteroaryl, heteroarylalkyl, etc.,] and their pharmaceutically acceptable salts were prepared. For example, electrophilic substitution of aminocyclopropane with compound I [X = Cl; R2 = 2-fluorobenzyl], e.g., prepared from 5-aminoimidazole-4-carboxamide hydrochloride in 3-steps, followed by acid work-up furnished compound I [R1 = cyclopropyl; R2 = 2-fluorobenzyl] methanesulfonate in 80.3% overall yield. In human PDE-4 inhibition assays, compds. I showed indicative (sic.) inhibition of PDE-4 activity (no data provided). Compds. I are claimed useful for the treatment of psychosis, Alzheimer's disease, allergy, inflammation, etc.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD
 (5 CITINGS)
 REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 40 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2004:80659 CAPLUS
 DOCUMENT NUMBER: 140:146131
 TITLE: Preparation of 6-amino-1H-indazole and 4-aminobenzofuran derivatives useful as phosphodiesterase 4 inhibitors
 INVENTOR(S): Schumacher, Richard A.; Hopper, Allan T.; Tehim, Ashok
 PATENT ASSIGNEE(S): Memory Pharmaceuticals Corporation, USA
 SOURCE: PCT Int. Appl., 75 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004009557	A1	20040129	WO 2003-US22401	20030718
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US 20030149052	A1	20030807	US 2003-361634	20030211
CA 2492911	A1	20040129	CA 2003-2492911	20030718
AU 2003256601	A1	20040209	AU 2003-256601	20030718
US 20040087584	A1	20040506	US 2003-622117	20030718
US 7153871	B2	20061226		
EP 1549619	A1	20050706	EP 2003-765684	20030718
EP 1549619	B1	20090121		
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BR 2003013000	A	20050712	BR 2003-13000	20030718
CN 1668602	A	20050914	CN 2003-817233	20030718
CN 100381425	C	20080416		
JP 2006502995	T	20060126	JP 2004-523528	20030718
NZ 537725	A	20060831	NZ 2003-537725	20030718
NZ 547469	A	20071130	NZ 2003-547469	20030718
AT 421505	T	20090215	AT 2003-765684	20030718
CN 101423497	A	20090506	CN 2008-10108288	20030718
RU 2354648	C2	20090510	RU 2005-104820	20030718
ES 2323688	T3	20090723	ES 2003-765684	20030718
IN 2005DN00076	A	20081107	IN 2005-DN76	20050107
ZA 2005000436	A	20060726	ZA 2005-436	20050117
MX 2005000825	A	20050829	MX 2005-825	20050119
NO 2005000871	A	20050218	NO 2005-871	20050218
HK 1081194	A1	20080905	HK 2006-101282	20060127
US 20070078139	A1	20070405	US 2006-602283	20061121
US 20070123570	A1	20070531	US 2006-642592	20061221
PRIORITY APPLN. INFO.:			US 2002-396726P	P 20020719
			US 2001-262651P	P 20010122
			US 2001-267196P	P 20010208
			US 2001-306140P	P 20010719
			US 2002-51309	A3 20020122
			CN 2003-817233	A3 20030718
			NZ 2003-537725	A3 20030718
			US 2003-622117	A3 20030718
			WO 2003-US22401	W 20030718
			US 2004-754600	A3 20040112

OTHER SOURCE(S): MARPAT 140:146131
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention refers to new aminoindazole and aminobenzofuran derivs. of formula I and II [wherein: R1 = H, (un)substituted (cyclo/hetero)alkyl; R2 = H, (un)substituted alkyl; R3 = H, (un)substituted alkyl, arylalkyl, etc.; R4 = H, (un)substituted (hetero)aryl; R5 = (halo)alkoxy, (halo)alkylthio; R6 = (un)substituted -C(O)-alkyl, etc.] useful as phosphodiesterase 4 (PDE4) inhibitors. In vitro measurements of human type 4 phosphodiesterase inhibition activity and in vivo tests for

learning and memory (passive avoidance in rats and radial arm maze task in rats) were performed for compds. I and II. Compds. I and II are claimed to be useful for treatment of patients suffering from memory impairment due to Alzheimer's diseases, schizophrenia, Parkinson's disease, etc. For instance, indazole III (example 4) was prepared from 3-pyridinecarboxaldehyde and aminoindazole IV via reductive amination, amination of 3-IC₆H₄CO₂t-Bu by resultant amine V, and hydrolysis.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD
(3 CITINGS)

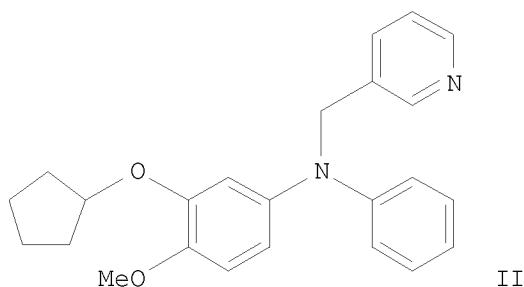
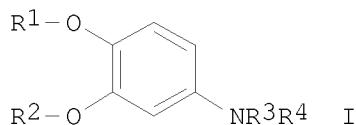
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 41 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:80654 CAPLUS
DOCUMENT NUMBER: 140:128150
TITLE: Preparation of selective phosphodiesterase 4 inhibitors, including ether-functionalized N-substituted aniline and diphenylamine analogs, for cognition enhancement and other uses
INVENTOR(S): Schumacher, Richard A.; Hopper, Allen T.; Tehim, Ashok; Hess, Hans-Jurgen Ernst; Unterbeck, Axel; Kuester, Erik; Brubaker, William Frederick, Jr.; Dunn, Robert F.
PATENT ASSIGNEE(S): Memory Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 199 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009552	A1	20040129	WO 2003-US22543	20030721
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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CA 2492907	A1	20040129	CA 2003-2492907	20030721
AU 2003256616	A1	20040209	AU 2003-256616	20030721
AU 2003256616	B2	20090827		
US 20050119225	A1	20050602	US 2003-622833	20030721
US 7405230	B2	20080729		
BR 2003012999	A	20050607	BR 2003-12999	20030721
EP 1539697	A1	20050615	EP 2003-765748	20030721
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1688545	A	20051026	CN 2003-822354	20030721
JP 2006504656	T	20060209	JP 2004-523585	20030721
NZ 537724	A	20061027	NZ 2003-537724	20030721
RU 2368604	C2	20090927	RU 2005-104819	20030721
IN 2005DN00091	A	20060609	IN 2005-DN91	20050110
ZA 2005000488	A	20060628	ZA 2005-488	20050118
MX 2005000827	A	20050829	MX 2005-827	20050119
NO 2005000870	A	20050331	NO 2005-870	20050218
IN 2007DN04839	A	20070824	IN 2007-DN4839	20070622

US 20090048255	A1	20090219	US 2008-174714	20080717
PRIORITY APPLN. INFO.:			US 2002-396725P	P 20020719
			US 2003-622833	A3 20030721
			WO 2003-US22543	W 20030721
			IN 2005-DN91	A3 20050110

OTHER SOURCE(S): MARPAT 140:128150
GI



AB PDE4 inhibition (no data) is achieved by novel compds., e.g., ether-functionalized N-substituted aniline and diphenylamine analogs (shown as I; variables defined below; e.g. II). Although the methods of preparation are not claimed, >40 example preps. are included. For example, II was prepared by arylation of N-[(3-pyridyl)methyl]-3-cyclopentyloxy-4-methoxyaniline by iodobenzene using NaOtBu, Pd2dba3, and PtBu3 in toluene. In a 'passive avoidance in rats' test, an in vivo test for learning and memory, the amnesic effect of MK-801 is reversed in a statistically significant manner by actual test compds. in a dose-dependent fashion [e.g., 3-cyclopentyloxy-4-methoxy-N-(3-pyridylmethyl)diphenylamine, ED range = 0.5 to 2.5 mg/kg, i.p.; and N-(3-cyclopentyloxy-4-methoxyphenyl)-N-(3-pyridylmethyl)-3-aminobenzoic acid, ED range = 0.1 to 2.5 mg/kg, i.p.]. In a 'radial arm maze task in rats' test, an in vivo test for learning and memory, the amnesic effect of MK-801 on working memory is reversed in a statistically significant manner by the administration of actual test compds. in a dose-dependent fashion [e.g., 3-cyclopentyloxy-4-methoxy-N-(3-pyridylmethyl)diphenylamine, ED = 2.5 mg/kg, i.p.; p<0.01]. For I: R1 is H, alkyl having 1-4 C atoms (un)substituted by ≥1 halo; R2 is C1-12 alkyl, C3-10 cycloalkyl, C4-16 cycloalkylalkyl, C6-14 aryl, C6-14-aryl-C1-5-alkyl, a partially unsatd. carbocyclic group having 5-14 C atoms, a C5-10 heterocyclic group, or a heterocycle-alkyl group; R3 is H, C1-8 alkyl, a partially unsatd. carbocycle-alkyl group, C7-19-aryl-C1-5-alkyl, or heteroarylalkyl; R4 is H, C3-10 cycloalkyl, C6-14 aryl, or heteroaryl having 5-10 ring atoms; addnl. details are given in the claims.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD
(9 CITINGS)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

DOCUMENT NUMBER: 140:59526
 TITLE: Preparation of 8-(biaryl)quinolines as PDE4
 inhibitors
 INVENTOR(S): Deschenes, Denis; Dube, Daniel; Dube, Laurence;
 Gallant, Michel; Girard, Yves; Lacombe, Patrick;
 MacDonald, Dwight
 PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
 SOURCE: PCT Int. Appl., 122 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000814	A1	20031231	WO 2003-CA957	20030623
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2490043	A1	20031231	CA 2003-2490043	20030623
AU 2003243870	A1	20040106	AU 2003-243870	20030623
AU 2003243870	B2	20081120		
EP 1517895	A1	20050330	EP 2003-760540	20030623
EP 1517895	B1	20070314		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006502104	T	20060119	JP 2004-514482	20030623
AT 356808	T	20070415	AT 2003-760540	20030623
ES 2282667	T3	20071016	ES 2003-760540	20030623
US 20050234238	A1	20051020	US 2004-517416	20041208
US 7153968	B2	20061226		
PRIORITY APPLN. INFO.:			US 2002-391364P	P 20020625
			US 2002-428313P	P 20021122
			WO 2003-CA957	W 20030623

OTHER SOURCE(S): MARPAT 140:59526
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

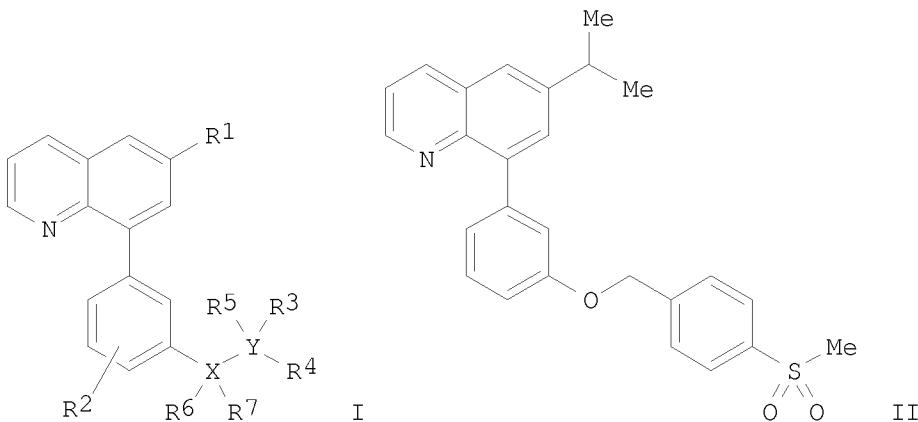
AB Title compds. I [wherein A = C or N; X = Ph, pyridyl, pyrazinyl, thiaphenyl, quinolinyl, benzofuranyl, oxadiazolyl, diazolylpyridinyl, imidazolylpyridinyl, oxadiazolylphenyl, benzodioxolyl; R1 = H, halo, or (un)substituted alkanoyl, cyclo/alkyl, alkenyl; R2, R3 = independently H, halo, OH, CN, NO₂, or dialkenyl/dicycloalkyl/alkyl, alkenyl, wide variety of C-containing and heteroat. groups and/or functional groups optionally linked by C1-4alkyl; R2 optionally forms a double bond with an adjoining bond; R4 = H, halo; any ring nitrogen optionally forms N-oxide and N-chloride; and pharmaceutically acceptable salts thereof] were prepared as phosphodiesterase IV (PDE4) inhibitors. For example, II was prepared by Suzuki cross-coupling of quinoline III with 2-bromo-3-chlorothiophene. One hundred fifty-five invention compds.

suppressed PDE4 with IC₅₀ values ranging from 36 μM to 0.005 μM in assays evaluating LPS- and FMLP-induced inhibition of tumor necrosis factor α (TNF-α) and leukotriene B₄ (LTB₄) in human whole blood. In a test measuring IgE-mediated allergic pulmonary inflammation induced by inhalation of antigen by sensitized guinea pigs, administration of I resulted in a significant reduction in the eosinophilia and the accumulation of other inflammatory leukocytes and effected less inflammatory lung damage. One hundred fifty-five invention compds. also inhibited the hydrolysis of cAMP to AMP by human recombinant phosphodiesterase IVa with IC₅₀ values ranging from 160 nM to 0.086 nM. Thus, I and their pharmaceutical compns. are useful for the treatment or prevention of a variety of allergic, inflammatory, CNS, and other conditions (no data).

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
(1 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 43 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:757679 CAPLUS
DOCUMENT NUMBER: 139:276825
TITLE: Preparation of 8-arylquinoline PDE4 inhibitors
INVENTOR(S): Gallant, Michel; Lacombe, Patrick; Dube, Daniel; Deschenes, Denis; MacDonald, Dwight; Dube, Laurence
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 184 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003078397	A1	20030925	WO 2003-CA374	20030317
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2479069	A1	20030925	CA 2003-2479069	20030317
AU 2003209896	A1	20030929	AU 2003-209896	20030317
EP 1487797	A1	20041222	EP 2003-744288	20030317
EP 1487797	B1	20090527		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 432261	T	20090615	AT 2003-744288	20030317
US 20050245513	A1	20051103	US 2004-508261	20040917
US 7144896	B2	20061205		
PRIORITY APPLN. INFO.:			US 2002-365088P	P 20020318
			WO 2003-CA374	W 20030317
OTHER SOURCE(S): GI	MARPAT	139:276825		



AB Title compds. I [wherein R1 = H, halo, or (un)substituted alkanoyl, (cyclo)alkyl, alkenyl, alkoxy, (hetero)aryl, CN, heterocycloalkyl, carbamoyl, sulfamoyl, etc.; R2 = H, halo, OH, or (un)substituted alkyl or alkoxy; R3 = absent or H, CO₂H, or (un)substituted (cycloalkyl)alkyl, alkanoyl, benzoyl, carbamoyl, etc.; R4 = (un)substituted Ph, pyrazolopyrimidinyl, benzothiazolyl, quinazolinyl, or heteroaryl; R5 = absent or H; R6 = absent, H, or alkyl; R7 = absent or H; X = O, S, N, C, or CO; wherein when X = O, S, or CO, then R6 and R7 are absent and when X = N, then R7 is absent; Y = C, S, N, SO₂, O, or CO; wherein when Y = S, SO₂, O, or CO, then R3 and R5 are absent and when Y = N, then R5 is absent; and pharmaceutically acceptable salts thereof] were prepared as phosphodiesterase IV (PDE4) inhibitors. For example, 3-(6-isopropylquinolin-8-yl)phenol was coupled with 1-chloromethyl-4-methanesulfonylbenzene in acetone to give II. One hundred sixteen invention compds. suppressed PDE4 with IC₅₀ values ranging from 80 μM to 0.029 μM in assays evaluating LPS- and FMLP-induced inhibition of tumor necrosis factor α (TNF-α) and leukotriene B4 (LTB4) in human whole blood. In a test measuring IgE-mediated allergic pulmonary inflammation induced by inhalation of antigen by sensitized guinea pigs, administration of I resulted in a significant reduction in the eosinophilia and the accumulation of other inflammatory leukocytes and effected less inflammatory lung damage. One hundred forty-one invention compds. also inhibited the hydrolysis of cAMP to AMP by human recombinant phosphodiesterase IVa with IC₅₀ values ranging from 150 nM to 0.056 nM. Thus, I and their pharmaceutical compns. are useful for the treatment or prevention of a variety of allergic, inflammatory, CNS, and other conditions (no data).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT.

L7 ANSWER 44 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:656587 CAPLUS

DOCUMENT NUMBER: 139:197374

DOCUMENT NUMBER: 109-19787
TITLE: Preparation of nicotinamides useful as PDE4 inhibitors for treating diseases including

INVENTOR(S): inflammatory, allergic and respiratory diseases
Bailey, Simon; Gautier, Elisabeth Colette Louise;
Henderson Alan John; Magee Thomas Victor; Marfat

PATENT ASSIGNEE(S): Monaghan, Sandra Marina; Stammen, Blanda Luzia Christa
Pfizer Limited, UK; Pfizer Inc.

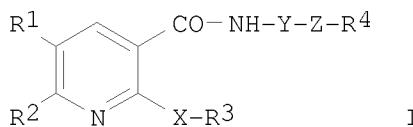
SOURCE: PCT Int. Appl., 266 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068235	A1	20030821	WO 2003-IB439	20030203
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2475712	A1	20030821	CA 2003-2475712	20030203
AU 2003245711	A1	20030904	AU 2003-245711	20030203
EP 1476158	A1	20041117	EP 2003-739392	20030203
EP 1476158	B1	20071114		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007564	A	20041221	BR 2003-7564	20030203
JP 2005522450	T	20050728	JP 2003-567417	20030203
CN 1652782	A	20050810	CN 2003-808186	20030203
NZ 534197	A	20070126	NZ 2003-534197	20030203
AT 378049	T	20071115	AT 2003-739392	20030203
ES 2292988	T3	20080316	ES 2003-739392	20030203
US 20030220361	A1	20031127	US 2003-360100	20030206
US 20030220366	A1	20031127	US 2003-361062	20030206
US 6949573	B2	20050927		
US 20040224975	A1	20041111	US 2004-865263	20040609
US 7060717	B2	20060613		
IN 2004DN02070	A	20050401	IN 2004-DN2070	20040719
MX 2004007737	A	20041015	MX 2004-7737	20040810
NO 2004003793	A	20041021	NO 2004-3793	20040910
US 20060014780	A1	20060119	US 2005-229395	20050916
ZA 2004005803	A	20060531	ZA 2004-5803	20060316
PRIORITY APPLN. INFO.:				
		GB 2002-3196	A	20020211
		GB 2002-20999	A	20020910
		GB 2002-24453	A	20021021
		GB 2002-27139	A	20021120
		US 2002-361991P	P	20020305
		GB 2002-20984	A	20020910
		US 2002-414247P	P	20020926
		US 2002-414304P	P	20020926
		GB 2002-24454	A	20021021
		US 2002-425406P	P	20021112
		US 2002-425474P	P	20021112
		GB 2002-27140	A	20021120
		US 2002-433330P	P	20021213
		US 2002-433336P	P	20021213
		WO 2003-IB439	W	20030203
		US 2003-361062	A3	20030206
		US 2004-865263	A1	20040609

OTHER SOURCE(S): MARPAT 139:197374
 GI



AB The invention relates to nicotinamides (shown as I; variables defined below; e.g. anti-2-(benzo[1,3]dioxol-5-yloxy)-N-[4-(2-hydroxybenzoylamino)cyclohexyl]nicotinamide) and to processes for the preparation of, intermediates used in the preparation of, compns. containing and the

uses of, such derivs. The nicotinamide derivs. according to the present invention are phosphodiesterase-4 inhibitors and are useful in numerous diseases, disorders and conditions, in particular inflammatory, allergic, respiratory diseases, disorders and conditions, as well as wounds. For I: R1 and R2 = H, halo, cyano, (C1-C4)alkyl and (C1-C4)alkoxy; X is -O-, -S- or -NH-; R3 = Ph, naphthyl, heteroaryl and (C3-C8)cycloalkyl or the bicyclic groups benzodioxol-5-yl, benzofuran-5-yl, benzofuran-6-yl, indan-5-yl; Y = 4-HNcyclohexyl, piperidin-1,4-diyl, 8-azabicyclo[3.2.1]octane-3,8-diyl, and 4-R5Ncyclohexyl wherein in each the N is bonded to Z in I and R5 = (C1-C4)alkyl and phenyl(C1-C4)alkyl. Z = C(O), C(O)NH, SO₂, SO₂NH, C(O)CH₂NHSO₂, SO₂NHC(O), C(O)CH₂NHC(O) wherein the left end is bonded to Y and the other end to R4; or alternatively Y-Z together = 4-NHC(O)cyclohexyl; R4 = Ph, naphthyl heteroaryl and (C3-C8)cycloalkyl, (un)substituted (C1-C6)alkyl; addnl. details including provisos are given in the claims. The antiinflammatory properties of 72 examples of I are demonstrated by their ability to inhibit TNF α release from human peripheral blood mononuclear cells, e.g. IC₅₀ = 0.014 nM for syn-2-(3,4-difluorophenoxy)-5-fluoro-N-[4-(2-hydroxy-5-methylbenzoylamino)cyclohexyl]nicotinamide. About 200 example preps. of I and 75 of intermediates are included. For example, to prepare anti-2-[(benzo[1,3]dioxol-5-yl)oxy]-N-[4-[(2-hydroxybenzoyl)amino]cyclohexyl]nicotinamide (160.7 mg), 2-hydroxybenzoic acid (0.767 mmol), 1-hydroxybenzotriazole hydrate (1.15 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.15 mmol) were stirred in DMF (5 mL) under an atmospheric of N₂ at room temperature for 1.5 h.

Anti-N-(4-aminocyclohexyl)-2-[(benzo[1,3]dioxol-5-yl)oxy]nicotinamide hydrochloride (0.767 mmol; preparation given) and N-methylmorpholine (0.767 mmol) were then added, and the reaction mixture stirred at room temperature for a

further 18 h.

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD
(6 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

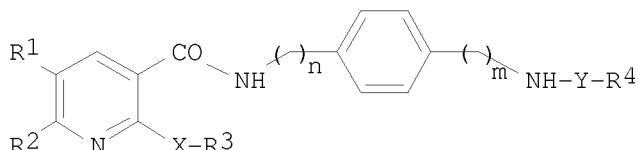
L7 ANSWER 45 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:656584 CAPLUS
DOCUMENT NUMBER: 139:197372
TITLE: Preparation of nicotinamides as phosphodiesterase-4 inhibitors for the treatment of diseases including inflammatory, allergic and respiratory diseases
INVENTOR(S): Magee, Thomas Victor
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068232	A1	20030821	WO 2003-IB377	20030203
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2475708	A1	20030821	CA 2003-2475708	20030203
AU 2003202116	A1	20030904	AU 2003-202116	20030203
EP 1476157	A1	20041117	EP 2003-700974	20030203
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007574	A	20041221	BR 2003-7574	20030203
JP 2005522449	T	20050728	JP 2003-567414	20030203
US 20030191158	A1	20031009	US 2003-360122	20030206
US 20030195233	A1	20031016	US 2003-361083	20030206
US 6756392	B2	20040629		
MX 2004007736	A	20041015	MX 2004-7736	20040810
PRIORITY APPLN. INFO.:			GB 2002-3193	A 20020211
			US 2002-362154P	P 20020305
			WO 2003-IB377	W 20030203

OTHER SOURCE(S): MARPAT 139:197372

GI



AB The invention relates to nicotinamides (shown as I; variables defined below; e.g. 2-(4-fluorophenoxy)-N-[4-[(2-hydroxy-3-methylbenzoylamino)methyl]benzyl]nicotinamide) and to processes for the preparation of, compns. containing and the uses of, such derivs. The nicotinamides

are phosphodiesterase-4 inhibitors and are useful in numerous diseases, disorders and conditions, in particular inflammatory, allergic and respiratory diseases, disorders and conditions as well as for wounds healing. Eighteen example prepns. of I and 10 of intermediates are included. For example, to prepare 2-(4-fluorophenoxy)-N-[4-[(2-hydroxy-3-methylbenzoylamino)methyl]benzyl]nicotinamide (80 mg), a solution of 2-hydroxy-3-methylbenzoic acid (0.773 mmol), 1-hydroxybenzotriazole (1.16 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.01 mmol), N-(4-aminomethylbenzyl)-5-fluoro-2-(4-fluorophenoxy)nicotinamide hydrochloride (0.773 mmol) (preparation described) and N-methylmorpholine (1.55 mmol) in DMF (6 mL) were stirred under N₂ at room temperature for 18 h. All the

examples were tested in an assay of inhibition of TNF α release from human peripheral blood mononuclear cells and found to have an IC₅₀ < 500 nM; most of the tested compds. have an IC₅₀ < 200 nM. For I: m = 0-3; n = 0-3; R1 and R2 = H, halo, cyano, (C₁-C₄)alkyl and (C₁-C₄)alkoxy; X is -O-,

-S- or -NH-; R3 = (a) Ph, naphthyl, heteroaryl and (C3-C8)cycloalkyl, each (un)substituted with 1 to 3 substituents each halo, cyano, (C1-C4)alkyl, (C1-C4)alkoxy, (C1-C4)thioalkyl, -C(O)NH₂, -C(O)NH[(C1-C4)alkyl], hydroxy, -O-C(O)(C1-C4)alkyl, -C(O)-O-(C1-C4)alkyl and hydroxy (C1-C4)alkyl, or (b) the bicyclic groups benzodioxol-5-yl, benzofuran-5-yl, benzofuran-6-yl, indan-5-yl; Y = -C(O)-, -C(O)NH-, -SO₂-, -SO₂NH-, -C(O)CH₂NHSO₂-, -SO₂NHC(O)-, -C(O)CH₂NHC(O)- wherein the left-hand connection is to NH and the right-hand connection is to R4. R4 = (a) Ph, naphthyl and heteroaryl, each (un)substituted with 1 to 3 substituents = carboxylic acid, C(O)-O-(C1-C4)alkyl, halo, cyano, -C(O)NH₂, (C1-C4)alkyl, (C1-C4)alkoxy, (C1-C4)haloalkyl, hydroxy, and hydroxy(C1-C4)alkyl, or (b) (C1-C4)alkyl (un)substituted with a hydroxy, carboxylic acid, C(O)-O-(C1-C4)alkyl, Ph, naphthyl or heteroaryl group wherein said Ph, naphthyl and heteroaryl are each (un)substituted with 1 to 3 substituents = carboxylic acid, C(O)O(C1-C4)alkyl, halo, cyano, -C(O)NH₂, (C1-C4)alkyl or (C1-C4)alkoxy, (C1-C4)haloalkyl, hydroxy, and hydroxy(C1-C4)alkyl.

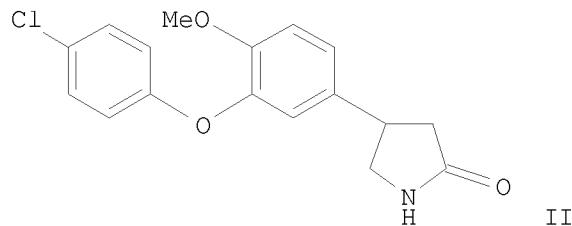
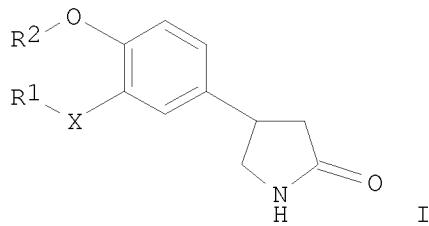
OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (12 CITINGS)
 REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 46 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2003:319707 CAPLUS
 DOCUMENT NUMBER: 138:321128
 TITLE: Preparation of 4-(4-alkoxy-3-hydroxyphenyl)-2-pyrrolidinone derivatives as PDE-4 inhibitors for the treatment of neurological syndromes
 INVENTOR(S): Liu, Ruiping; De Vivo, Michael; Hess, Hans-Jurgen Ernst; Hopper, Allen; Keuster, Erik; Tehim, Ashok
 PATENT ASSIGNEE(S): Memory Pharmaceuticals Corporation, USA
 SOURCE: PCT Int. Appl., 160 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003032981	A1	20030424	WO 2002-US32834	20021016
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2463469	A1	20030424	CA 2002-2463469	20021016
AU 2002335015	A1	20030428	AU 2002-335015	20021016
AU 2002335015	B2	20061102		
US 20030139406	A1	20030724	US 2002-270724	20021016
US 7235579	B2	20070626		
EP 1435944	A1	20040714	EP 2002-801710	20021016
EP 1435944	B1	20090930		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002013660	A	20040824	BR 2002-13660	20021016

CN 1604776	A	20050406	CN 2002-825102	20021016
JP 2005508961	T	20050407	JP 2003-535784	20021016
NZ 532288	A	20051223	NZ 2002-532288	20021016
RU 2340600	C2	20081210	RU 2004-115333	20021016
KR 2009080573	A	20090724	KR 2009-714588	20021016
IN 2004DN00971	A	20050401	IN 2004-DN971	20040413
MX 2004003516	A	20040723	MX 2004-3516	20040415
ZA 2004002856	A	20050125	ZA 2004-2856	20040415
NO 2004002024	A	20040514	NO 2004-2024	20040514
US 20050272803	A1	20051208	US 2005-186958	20050722
IN 2008DN04357	A	20080815	IN 2008-DN4357	20080522
US 20090176799	A1	20090709	US 2008-325433	20081201
PRIORITY APPLN. INFO.:				
			US 2001-329314P	P 20011016
			US 2002-270724	A1 20021016
			WO 2002-US32834	W 20021016
			IN 2004-DN971	A3 20040413
			KR 2004-705475	A3 20040414
			US 2005-186958	A1 20050722

OTHER SOURCE(S): MARPAT 138:321128
GI



AB Title compds. I [X = O; R1 = alkyl, cycloalkyl, heterocyclic, etc.; R2 = alkyl; R3 = H, alkyl, cycloalkyl, arylalkyl, etc.] are prepared For instance, Me 3-(3-benzyloxy-4-methoxyphenyl)-4-nitrobutanoate is converted to 3-benzyloxy-4-methoxyphenyl (MeOH, NiCl₆, NaBH₄, 30 min, 0°) and subsequently debenzylated (MeOH/CH₂Cl₂, H₂-10% Pd/C, 20 psi, 8 h). This intermediate is then coupled to 4-chlorophenylboronic acid (CH₂Cl₂, Cu(OAc)₂, Et₃N, 18 h) to give II. I exhibit improved PDE4 inhibition as compared to rolipram and show selectivity with regard to inhibition of other classes of PDEs.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD
(4 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

DOCUMENT NUMBER: 138:73184
 TITLE: Preparation of substituted 8-arylquinoline phosphodiesterase-4 (PDE4) inhibitors
 INVENTOR(S): Dube, Daniel; Girard, Yves; MacDonald, Dwight;
 Mastracchio, Anthony; Gallant, Michel; Lacombe,
 Patrick; Deschenes, Denis
 PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
 SOURCE: PCT Int. Appl., 204 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003002118	A1	20030109	WO 2002-CA953	20020626
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2450686	A1	20030109	CA 2002-2450686	20020626
AU 2002344885	A1	20030303	AU 2002-344885	20020626
AU 2002344885	B2	20060629		
EP 1404330	A1	20040407	EP 2002-742600	20020626
EP 1404330	B1	20050601		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005501822	T	20050120	JP 2003-508357	20020626
AT 296630	T	20050615	AT 2002-742600	20020626
ES 2242036	T3	20051101	ES 2002-742600	20020626
US 20040162314	A1	20040819	US 2003-478791	20031125
US 6919353	B2	20050719		
PRIORITY APPLN. INFO.:				
		US 2001-301220P	P	20010627
		US 2001-303472P	P	20010706
		WO 2002-CA953	W	20020626

OTHER SOURCE(S): MARPAT 138:73184
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 8-Arylquinolines (shown as I; variables defined below; e.g. both enantiomers of 4-hydroxy-1-[3-[6-(1-methanesulfonyl-1-methylethyl)quinolin-8-yl]phenyl]-2-(4-methanesulfonylphenyl)-4-methylpentan-3-one) wherein the aryl group at the 8-position contains a meta two atom bridge to an optionally substituted Ph or pyridyl group, are PDE4 inhibitors useful to treat asthma, chronic bronchitis, chronic obstructive pulmonary disease, arthritis, respiratory distress syndrome, allergic rhinitis, neurogenic inflammation, pain, rheumatoid arthritis, and other diseases. R1-R7 and Ar are as in claim 1. For I: Ar is Ph, pyridinone, pyridyl, or pyridyl N-oxide, optionally substituted with 1-5 independent -Cl-6-alkyl, -OH, -CN, halogen, -CF₃, -(C₀-6-alkyl)-SOn-(C₁-6-alkyl), -(C₀-6-alkyl)-SOn-NH-(C₁-6-alkyl) or 5-membered heteroaryl ring containing 1-4 heteroatoms = O, S or N, wherein the 5-membered-ring is optionally

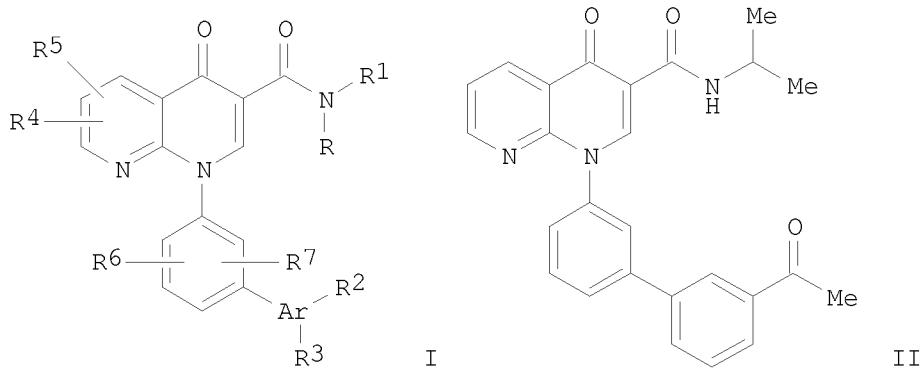
substituted. R1 is H, halogen; or a -C1-6-alkyl, -cycloC3-6alkyl, -C1-6-alkenyl, -C0-4alkyl-C(O)-C0-4alkyl, -C1-6-alkoxy, aryl, heteroaryl, -CN, -heterocycloC3-6-alkyl, -amino, -C1-6-alkylamino, -(C1-6-alkyl)(C1-6-alkyl)amino, -C1-6-alkyl(oxy)C1-6-alkyl, -C(O)NH(aryl), -C(O)NH(heteroaryl), -SOnNH(aryl), -SOnNH(heteroaryl), -SOnNH(C1-6-alkyl), -C(O)N(C0-6alkyl)(C0-6-alkyl), -NH-SOn-(C1-6-alkyl), -carbamoyl, -(C1-6-alkyl)-O-C(CN)dialkylamino, or -(C0-6-alkyl)-SOn-(C1-6-alkyl) group, wherein any of the groups is optionally substituted with 1-5 substituents. R2, R3, R6, and R7 = H, halogen, hydroxy, -C1-6-alkyl, or -C1-6-alkoxy, wherein the alkyl and alkoxy are optionally substituted independently with 1-3 halogen or OH; R4 is H, halogen, -CN, Ph, oxadiazolyl, or -C(O)-O-C0-6alkyl, wherein the alkyl and latter three possibilities are optionally substituted. R5 is H, hydroxy, -CN; or a -C1-6-alkyl, -C(O)C1-6alkyl, -C(O)aryl, -C(O)pyridyl, -C(O)-O-C0-6-alkyl, -C(O)-C3-7-cycloalkyl, -C1-6-alkyl-C3-7cycloalkyl, -C1-6-alkyl(C3-7-cycloalkyl)2, -C1-6-alkylaryl, -C(O)-N(C0-6alkyl)2, -SOnaryl, -SOn-C1-6-alkyl, -SOn-C3-7-cycloalkyl, -SOn-N(C0-6-alkyl)2, -P(O)(C1-6-alkyl)2, -P(O)(C1-6-alkoxy)2, Ph, pyridyl, -SOnimidazolyl, -SOnthiazolyl, 5-membered heteroaryl ring containing 1-4 heteroatoms = O, S or N or oxoisoxaphosphinanyl group, any of which group optionally substituted; or R5 and R6 form :O; or R6 and R3 form -CH2- or -O-; and n is 0-2. Although the methods of preparation are not claimed, >100 example preps. are included. The IC50 values for PDE4 inhibition of Examples 1-113 generally are 0.02-26 μM as measured using LPS and FMLP-induced TNF-α and LTB4 assays in human whole blood. I were tested for effects on an IgE-mediated allergic pulmonary inflammation induced by inhalation of antigen by sensitized guinea pigs;. Administration of I (0.001-10 mg/kg i.p. or p.o.), up to three times during the 48 h following antigen challenge, lead to a significant reduction in the eosinophilia and the accumulation of other inflammatory leukocytes. There was also less inflammatory damage in the lungs of animals treated with I. Compds. which inhibit the hydrolysis of cAMP to AMP by the type-IV cAMP-specific phosphodiesterases were screened in a 96-well plate format; IC50 values of I generally ranged 0.1-25 nM.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD
(4 CITINGS)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 48 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:906219 CAPLUS
DOCUMENT NUMBER: 138:4594
TITLE: Preparation of 1-biaryl-[1,8]naphthyridin-4-one phosphodiesterase IV inhibitors for treatment of asthma and inflammation
INVENTOR(S): Guay, Daniel; Girard, Mario; Hamel, Pierre; Laliberte, Sebastien; Friesen, Richard; Girard, Yves; Li, Chun
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 166 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002094823	A1	20021128	WO 2002-CA746	20020522
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,				

PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
 UG, US, UZ, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
 CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 CA 2447765 A1 20021128 CA 2002-2447765 20020522
 AU 2002257459 A1 20021203 AU 2002-257459 20020522
 AU 2002257459 B2 20061214
 EP 1397359 A1 20040317 EP 2002-727127 20020522
 EP 1397359 B1 20050831
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 JP 2004534773 T 20041118 JP 2002-591496 20020522
 AT 303384 T 20050915 AT 2002-727127 20020522
 ES 2247325 T3 20060301 ES 2002-727127 20020522
 US 20030096829 A1 20030522 US 2002-154591 20020524
 US 6677351 B2 20040113
 PRIORITY APPLN. INFO.: US 2001-293247P P 20010524
 OTHER SOURCE(S): MARPAT 138:4594 WO 2002-CA746 W 20020522
 GI



AB Title compds. I [wherein Ar = Ph, pyridyl, pyrimidyl, indolyl, quinolinyl, thienyl, pyridonyl, oxazolyl, oxadiazolyl, thiadiazolyl, imidazolyl, or heteroaryl oxides; R = H or alkyl; R1 = H or (un)substituted (cyclo)alkyl, alkoxy, alkenyl, alkynyl, heteroaryl, or heterocyclyl; R2 = H, halo, (cyclo)alkyl, alkoxy, amino, acyl, alkoxy carbonyl, alkylsulfamoyl, alkylsulfonyl, or (un)substituted Ph, heteroaryl, or heterocyclyl, etc.; R3 = H, OH, NH₂, halo, (un)substituted alkyl; R4-R7 = independently H, halo, NH₂, or (un)substituted alkyl or alkoxy; or pharmaceutically acceptable salts thereof] were prepared as phosphodiesterase IV (PDE4) inhibitors for the treatment of asthma and inflammation. For instance, Et 3-(3-bromoanilino)-2-(2-chloronicotinoyl)acrylate was cyclized using NaH in THF and the resulting ester saponified to give 1-(3-bromophenyl)-1,4-dihydro-[1,8]naphthyridin-4-one-3-carboxylic acid. Amidation with isopropylamine, followed by treatment with 3-acetylphenylboronic acid in the presence of trans-PdBr₂(PPh₃)₂ and Na₂CO₃ in toluene and EtOH gave II. I demonstrated PDE4 inhibitory activity by suppression of TNF- α secretion in LPS stimulated human blood with IC₅₀ values generally ranging from 0.005 μ M to 15.4 μ M. In a SPA based PDE activity assay, I inhibited the hydrolysis of cAMP to AMP by human recombinant phosphodiesterase IVa with IC₅₀ values between 34.3 nM and 134.0 nM.

OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD
(8 CITINGS)

REFERENCE COUNT:

4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 49 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2002:736215 CAPLUS
 DOCUMENT NUMBER: 137:247488
 TITLE: Preparation of C-organooxy- and N-substituted aniline and diphenylamine analogs as phosphodiesterase 4 inhibitors useful for enhancing cognition
 INVENTOR(S): Hopper, Allen; Schumacher, Richard A.; Tehim, Ashok; De Vivo, Michael; Brubaker, William Frederick, Jr.; Liu, Ruiping; Hess, Hans-Juergen Ernst; Unterbeck, Axel
 PATENT ASSIGNEE(S): Memory Pharmaceuticals Corporation, USA
 SOURCE: PCT Int. Appl., 131 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002074726	A2	20020926	WO 2002-US1508	20020122
WO 2002074726	A3	20030313		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2435847	A1	20020926	CA 2002-2435847	20020122
AU 2002303078	A1	20021003	AU 2002-303078	20020122
AU 2002303078	B2	20070830		
US 20020151566	A1	20021017	US 2002-51309	20020122
US 6699890	B2	20040302		
EP 1353907	A2	20031022	EP 2002-731078	20020122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 2003002793	A2	20031128	HU 2003-2793	20020122
HU 2003002793	A3	20060130		
EE 200300347	A	20031215	EE 2003-347	20020122
CN 1498211	A	20040519	CN 2002-807010	20020122
CN 100378075	C	20080402		
JP 2005507365	T	20050317	JP 2002-573735	20020122
JP 4223287	B2	20090212		
BR 2002006943	A	20060124	BR 2002-6943	20020122
NZ 527081	A	20060331	NZ 2002-527081	20020122
RU 2321583	C2	20080410	RU 2003-124303	20020122
US 20030149052	A1	20030807	US 2003-361634	20030211
US 20040087584	A1	20040506	US 2003-622117	20030718
US 7153871	B2	20061226		
BG 108003	A	20040930	BG 2003-108003	20030718
IN 2003DN01131	A	20070316	IN 2003-DN1131	20030718
NO 2003003288	A	20030922	NO 2003-3288	20030721
ZA 2003005623	A	20041117	ZA 2003-5623	20030721
KR 856622	B1	20080903	KR 2003-709624	20030721
MX 2003006519	A	20041015	MX 2003-6519	20030722
US 20040230072	A1	20041118	US 2004-754600	20040112

US 7205320	B2	20070417		
HK 1066215	A1	20080829	HK 2004-109061	20041117
US 20070078139	A1	20070405	US 2006-602283	20061121
IN 2008DN08577	A	20090515	IN 2008-DN8577	20081013
PRIORITY APPLN. INFO.:				
			US 2001-262651P	P 20010122
			US 2001-267196P	P 20010208
			US 2001-306140P	P 20010719
			US 2000-257196P	P 20001222
			US 2002-51309	A3 20020122
			US 2002-51390	A3 20020122
			WO 2002-US1508	W 20020122
			US 2002-396726P	P 20020719
			IN 2003-DN1131	A3 20030718
			US 2004-754600	A3 20040112

OTHER SOURCE(S): MARPAT 137:247488

AB Phosphodiesterase 4 (PDE4) inhibition is achieved by novel compds., 4-R1O-3-R2OC6H3NR3R4 (1, e.g., N-substituted aniline and diphenylamine analogs; e.g. 3-cyclopentyloxy-4'-ethyl-4-methoxy-N-(3-pyridylmethyl)diphenylamine). In 1, R1 is C1-4 alkyl unsubstituted or substituted one or more times by halogen. R2 is C1-12 alkyl, wherein optionally one or more -CH₂CH₂- groups is replaced in each case by -CH:CH- or -C.tpbond.C-, C3-10 cycloalkyl, C4-16 cycloalkylalkyl, C6-14 aryl, arylalkyl with C6-14 aryl and C1-5 alkyl, a partially unsatd. C5-14 carbocyclic group, a C5-10 heterocyclic group, which is saturated, partially saturated or unsatd., in which at least 1 ring atom is a N, O or S atom, or a heterocycloalkyl group with a C5-10 heterocyclic portion that is saturated, partially saturated or unsatd., in which at least 1 ring atom is a N, O or S atom, and a C1-5 alkyl portion. R3 is H, C1-8 (preferably C1-4) alkyl, a partially unsatd. carbocycle-alkyl group with a C5-14 carbocyclic portion and a C1-5 alkyl portion, C7-19 arylalkyl with C6-14 aryl and C1-5 alkyl, or heteroarylalkyl with C5-10 heteroaryl having at least 1 ring atom N, O or S atom and with C1-5 alkyl. R4 is H, C6-14 aryl or heteroaryl having 5 to 10 ring atoms in which at least 1 ring atom is a heteroatom. Addnl. restrictions on the values of R1-R4 are given in the claims. The amnesic effect of MK-801 on working memory in rats (radial arm maze task) is reversed in a statistically significant manner by the administration of actual test compds. in a dose-dependent fashion [e.g., 3-cyclopentyloxy-4-methoxy-N-(3-pyridylmethyl)diphenylamine, ED = 2.5 mg/kg, i.p.; p<0.01]. The amnesic effect of MK-801 on rats in a passive avoidance experiment is reversed in a statistically significant manner by actual test compds. in a dose-dependent fashion [e.g., 3-cyclopentyloxy-4-methoxy-N-(3-pyridylmethyl)diphenylamine, ED range = 0.5 to 2.5 mg/kg, i.p.; and N-(3-cyclopentyloxy-4-methoxyphenyl)-N-(3-pyridylmethyl)-3-aminobenzoic acid, ED range = 0.1 to 2.5 mg/kg, i.p.]. Although the methods of preparation are not claimed, .apprx.20 example preps. are included and hundreds of compds. are listed in the claims.

OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD
(6 CITINGS)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 50 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:695783 CAPLUS

DOCUMENT NUMBER: 137:216886

TITLE: Preparation of 8-(alkenylaryl)quinoline phosphodiesterase-4 inhibitors

INVENTOR(S): Vailaya, Anant; Conlon, David A.; Ho, Guo-Jie; Macdonald, Dwight; Perrier, Helene; Thibert, Roch; Kwong, Elizabeth; Clas, Sophie-Dorothee

PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Merck Frosst Canada & Co.

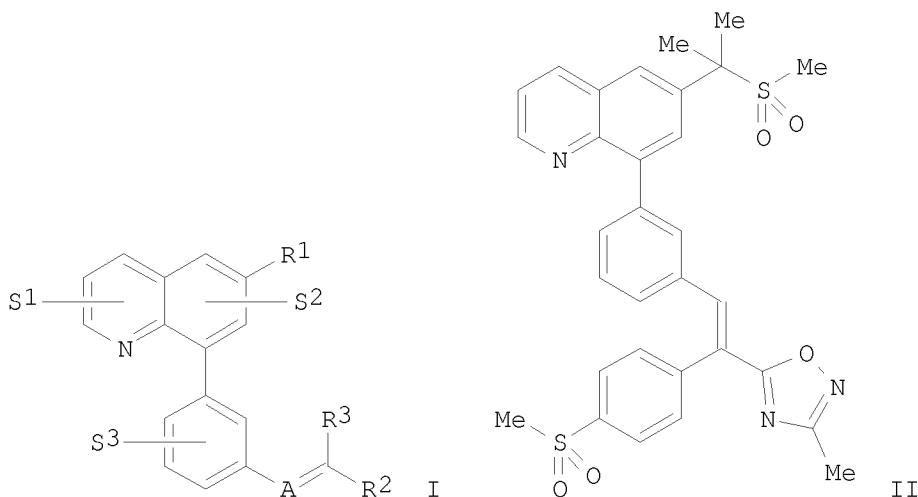
SOURCE: PCT Int. Appl., 110 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002069970	A1	20020912	WO 2001-US48674	20011214
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20020143032	A1	20021003	US 2001-40993	20011109
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CA 2431549	A1	20020912	CA 2001-2431549	20011214
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AU 2001297603	B2	20060216		
EE 200300266	A	20031015	EE 2003-266	20011214
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EP 1363635	B1	20090415		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001016372	A	20031209	BR 2001-16372	20011214
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NZ 526376	A	20050225	NZ 2001-526376	20011214
AT 428420	T	20090515	AT 2001-273908	20011214
BG 107900	A	20040630	BG 2003-107900	20030611
ZA 2003004672	A	20040421	ZA 2003-4672	20030617
NO 2003002807	A	20030815	NO 2003-2807	20030619
MX 2003005673	A	20031006	MX 2003-5673	20030619
IN 2003CN01089	A	20050422	IN 2003-CN1089	20030717
PRIORITY APPLN. INFO.:			US 2000-256803P	P 20001220
			WO 2001-US48674	W 20011214

OTHER SOURCE(S): MARPAT 137:216886
 GI



AB Title compds. I [wherein S1-S3 = independently H, OH, halo, NO₂, CN, or (un)substituted alkyl or alkoxy; R1 = H, OH, halo, or (un)substituted acyl, (cyclo)alkyl, alkenyl, alkoxy, (hetero)aryl, heterocycloalkyl, NH₂, carbamoyl, sulfamoyl, etc.; A = CH, C-ester, or CR₄; R2 and R3 = independently H, halo, CN, CO₂H, or (un)substituted (hetero)aryl, (heterocyclo)alkyl, alkoxy, acyl, carbamoyl, etc.; with the proviso that 1 of R2 and R3 must = (hetero)aryl; when R2 and R2 both = (hetero)aryl, then R2 and R3 may be optionally connected by a thio, oxy, or alkyl bridge to from a fused 3-ring system; R4 = CN or (un)substituted (hetero)aryl, alkyl, acyl, carbamoyl, etc.; or R2 or R3 may be optionally joined to R4 by a bond to form a ring; n = 0-2; and pharmaceutically acceptable H₂SO₄, methanesulfonic acid, p-toluenesulfonic acid, 2-naphthalenesulfonic acid, hydrochloride acid, or benzenesulfonic acid salts thereof] were prepared as phosphodiesterase-4 (PDE4) inhibitors. For example, a solution of (E)-1-(3-bromophenyl)-2-(3-methyl-1,2,4-oxadiazol-5-yl)-2-[4-(methylsulfonyl)phenyl]ethene, diboron pinacol ester, [1,1'-bis(diphenylphosphino)ferrocene]PdCl₂, and KOAc in DMF was stirred at 80° for 3 h. Sequential addition of 6-[1-methyl-1-(methylsulfonyl)ethyl]-8-bromoquinoline, [1,1'-bis(diphenylphosphino)ferrocene]PdCl₂, and Na₂CO₃ followed by heating at 80° overnight gave (E)- and (Z)-II. Forty-two compds. of the invention exhibited IC₅₀ values ranging from 0.04 μM to 8.71 μM in LPS and fMLP-induced TNF-α and LTB₄ assays performed on human whole blood. All but one of same compds. inhibited the hydrolysis of cAMP to AMP by type-IV cAMP-specific phosphodiesterases with IC₅₀ values ranging from 0.14 nM to 10.24 nM. Thus, I are useful as anti-inflammatory and anti-allergic agents for treatment of a wide variety of PDE4-related diseases and conditions (no data).

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD
(3 CITINGS)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 51 OF 51 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1997:751595 CAPLUS

DOCUMENT NUMBER: 128:97573

ORIGINAL REFERENCE NO.: 128:18944h,18945a

TITLE: Rolipram and its optical isomers, phosphodiesterase 4 inhibitors, attenuated the scopolamine-induced impairments of learning and memory in rats

AUTHOR(S): Egawa, Takashi; Mishima, Kenichi; Matsumoto, Yoshiaki;

CORPORATE SOURCE: Iwasaki, Kiyo; Iwasaki, Katsunori; Fujiwara, Michihiro
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SOURCE: Japanese Journal of Pharmacology (1997), 75(3),
275-281

CODEN: JJPAAZ; ISSN: 0021-5198

PUBLISHER: Japanese Pharmacological Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We investigated the effects of (\pm)-rolipram, a phosphodiesterase (PDE) 4 inhibitor, and its isomers on scopolamine-induced deficits of learning and memory in rats using an 8-arm radial maze task and a passive avoidance task. 1) In the 8-arm radial maze task, (\pm)-rolipram (0.02-0.2 mg/kg, p.o.), (-)-rolipram (0.01.apprx.0.02 and 0.02.apprx.0.5 mg/kg, p.o.) and (+)-rolipram (20-50 mg/kg, p.o.) attenuated the scopolamine-induced deficits of spatial cognition. As for the min. ED of each drug, (-)-rolipram was 2 and 2000 times as (\pm)-rolipram and (+)-rolipram, resp. (-)-Roliplram produced a biphasic dose-response and (\pm)-rolipram produced a broad dose-response. 2) (\pm)-Roliplram and its isomers also attenuated the scopolamine-induced deficits in the passive avoidance response. Also for the min. ED, (.apprx.)-rolipram (0.01 .apprx. 0.02 mg/kg) was 2 and 200 times as potent as (\pm)-rolipram (0.02.apprx.0.1 mg/kg) and (+)-rolipram (2 mg/kg). 3) The behaviorally EDs of (\pm)-rolipram and its isomers also enhanced the oxotremorine-induced tremors in mice. Comparing these racemic isomers, (-)- and (\pm)-rolipram have more potent effects than (+)-rolipram on scopolamine-induced deficits in the 8-arm radial maze task and passive avoidance task. Especially (\pm)-rolipram has a wide dose range in these behavioral study. These results suggest that the ameliorating effects of rolipram might result from the indirect potentiation of various transmitters including cholinergic and noradrenergic systems by an increase in cAMP with the inhibition of PDE4.

OS.CITING REF COUNT: 36 THERE ARE 36 CAPLUS RECORDS THAT CITE THIS RECORD (36 CITINGS)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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